ROLE OF NIFEDIPINE IN PRETERM LABOUR

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CERTIFICATE

This is to certify that this dissertation entitled "**ROLE OF NIFEDIPINE IN PRETERM LABOUR**" submitted by **Dr. M.RATHNA,** appearing for part II M.D. Branch II Obstetrics and Gynaecology Degree examination in March 2010, is a bonafide record of work done by her under my direct guidance and supervision as per the rules and regulations of the Tamil Nadu Dr. M.G.R. Medical University Chennai, Tamil Nadu, India. I forward this dissertation to the Tamil Nadu Dr. M.G.R. Medical University Chennai, India.

Professor and Head of Department
Department of Obstetrics and Gynaecology,
Government RSRM Lying in Hospital,
Stanley Medical College,
Chennai -600 001

THE DEAN

Stanley Medical College
Chennai - 600 001

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INTRODUCTION

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Preterm labour and delivery before 37 weeks of gestation is a principal contributor to perinatal mortality and morbidity. Despite advances in perinatal medicine in recent decades the problems of preterm delivery continues to frustrate satisfactory reproductive outcomes with little progress having been made in identifying and reducing the frequency of preterm birth.

However a real reduction in preterm delivery rates will only take place through an improved understanding of the physiology of labour, identification of patients at risk, prediction and prevention of its occurrence, early detection of its onset and effective tocolysis.

Rush et al, reported that 85% of neonatal deaths not due to lethal congenital malformations occur in infants with gestational age between 32 and 37 weeks. While the survival rate has improved greatly over the last three decades the incidence of major handicaps remains unchanged at 6-7% of all preterm births.

The social and emotional cost of perinatal mortality and morbidity associated with preterm birth is immeasurable. Ideally preterm labour should be prevented. However pharmacological inhibition of preterm labour

remains the most effective means to delay delivery and improve neonatal outcome until a more effective means of prevention is identified. Our study is concerned with the role of the calcium channel blocker,nifedipine in preterm labour as a tocolytic agent.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

DEFINITION

Preterm labour is defined as the onset of regular, painful, frequent uterine contractions causing progressive effacement and dilatation of cervix occurring before 37 completed weeks of gestation from the first day of last menstrual period (Anderson 1977).An infant born before 37 completed weeks should be called preterm (WHO 1969,ACOG 1995).

The lower limit which correlates with the fetal viability is less clearly defined. In United States it is 20 weeks (ACOG, 1995). Royal College of Obstetricians and Gynecologists (RCOG) Working Party considered it as 24 weeks. FIGO defined it as 22 weeks of above. In India, for legal purpose of viability it is defined as any gestation carried beyond 28 weeks (196 days).

INCIDENCE

The incidence of preterm delivery rates is developed countries lies between 5% and 10%(Rush et al1979, NewZealand Health Statistics report 1978). The incidence in India being 10-14% (FOGSI).

IMPACT OF PRETERM BIRTH

The most common maternal complication is postpartum endometritis which usually responds to antibiotics. Maternal mortality and morbidity as a consequence of preterm labour is rare (Fernando Arias ,3rd ed).

Risks of Preterm Infant

Aside from survival, appreciable physical and intellectual compromise afflicts preterm infants.

- Birth asphyxia
- RDS (Respiratory Distress Syndrome)
- Apnoea of prematurity
- Jaundice
- Hemorrhage
- Sepsis
- Shock
- Hypothermia
- Metabolic problems (hypoglycemia)
- Intraventricular hemorrhage(Germinal matrix hemorrhage)
- Neonatal encephalopathy (Cerebral palsy /periventricular leukomalacia)
- Necrotising enterocolitis

- Patent ductus arteriosus
- Retrolental fibroplasia
- Sensorineural deafness
- Recurrent respiratory infections
- Bronchopulmonary dysplasia
- Developmental delay
- Learning difficulties
- Reduced growth potential
- Enforced separation of baby and mother
- Feeding difficulties

The cost of preterm birth can be measured in terms of mortalitiy and morbidity and in short term and long term financial costs which increase with lower gestational age.Levit and coworkers(1995)found that more than a third of the dollars expended for infant health care during the first year of life is spent on the 7% of neonates born who weigh less than 2500gm. The components of the costs are nursery, medical staff, stay in neonatal intensive care unit and treatment such as ventilation, artificial surfactant, recombinant erythropoietin and surgical procedures. The long term financial implications are unknown if the child is handicapped either physical or mental.

ETIOLOGY

Only when the factors causing prematurity are clearly understood any intelligent attempt at prevention can be made.

Nearly 50-60% preterm births occur following spontaneous labour, 30% is due to preterm rupture of membranes and rest are iatrogenic (Goldenberg RL 2002; Leitich H. 2005).

Meis and colleagues 1995b analysed the causes and found one third were indicated deliveries for maternal or fetal benefit.

One of the major reasons for increase in incidence of preterm birth is increase in multiple pregnancies (fertility drugs and artificial reproductive technology) and increased surveillance and intervention in high risk pregnancies (Ian Donald 6th ed).

Infections

a) Uterine

Bobitt and Ledger first suggested that unrecognized chorioamnionitis may be causally related to preterm labour. They documented positive cultures via transcervical needle aspiration or intrauterine catheters. As many as 50% of spontaneous preterm birth may be associated with infection

(Klein LL, Gibbs RS 2005). The common pathway of intrauterine infection is the ascending route.

Colonization of genital tract with group B streptococcus infection is associated with preterm labour (Bobitt et al, Lamont et al.,).

Colonization with Chlamydia trichomatis (Martin et al., Harrison et al.,) Mycoplasma hominis and Ureaplasma urealyticum (Klein et al., 2005) is associated with preterm labour .

Asymptomatic bacterial vaginosis and Trichomonas vaginalis confers a modest risk of spontaneous preterm labour . Bacterial vaginosis (Gravett et al) has association with low birth weight.

Edward et al., reported higher incidence of positive gonorrhea culture in preterm labour.

b**) Extrauterine**

Especially urinary tract infections. High prematurity rate is associated with asymptomatic bacteruria (Robertson et al).

Other are systemic illness like pneumonia, pyelonephritis. Periodontal disease is associated with preterm labour (Xiong X 2006) .

2. Placental

- Abnormal placentation (Causing decreased uteroplacental blood flow)
- Anatomical abnormalities
- Placental praevia
- Abruptio placenta

3. Uterine

- Congenital abnormalities 1-3% (particularly septate and bicornuate uterus).
- Incompetent Cervix and Cervical anatomical abnormalities
- Overdistention of uterus

4.Genetic (Genes for decidual relaxin /Fetal mitochondrial trifuntional protein defect, IL-1, β2 adrenergic receptor gene , tumor necrosis factor –α are implicated)

5.Vaginal bleeding in early pregnancy is associated with preterm labour (Williams Obsterics, 22nded).

6.Fetal

Congenital anomalies

7.Preterm labour of unknown origin(20-30%)

PATHOPHYSIOLOGY

The control of parturition is achieved by complex integration of endocrine, paracrine and autocrine mechanism.

The fetal pituitary adrenal axis needs to be intact (Gonik B et al). Stress induced release of corticotrophin releasing harmone (CRH) initiates parturition.

When fetal adrenal axis becomes more sensitive to ACTH there is increase in cortisol production, which leads to increased 17-hydroxylase and finally decreased progesterone.

Differential production of PGE_2 and $PGF_{2\alpha}$ by the three enzymes-phospholipases, PGH_2 synthase, 15 hydroxy prostaglandin dehydrogenase may be key in the balance between uterine quiescence and activity. This decidual activation and production of uterotropins is the penultimate event in initiation of labour .

Cox and colleges (1993) found that cytokines (1LI, 1L6, TNFδ, IL8) are released when there is inflammatory response to infection and intrauterine bleeding. These inturn stimulate arachidonic acid and prostaglandin production.

EPIDEMIOLOGY

1. Race

The incidence is greater among black women (Varner et al 2005).

2. Age

It is more common in extremes of age.Lumley JM et al 1993, reported high incidence of preterm delivery in women under 17 years and over 35 years.

3. Weight

Poor nutrition, prepregnancy weight and weight gain during pregnancy play a important role in causing preterm birth. Hickly and colleagues 1995, have shown low maternal prenatal gain is specifically associated with preterm birth.

4. Stature

Short statured mother have more tendency to produce smaller babies.

5. **Socio- Economic Status**

Women from lower socio economic status tends to be less educated and would not have satisfactory general, perinatal and antenatal care (Goffinet F 2005).

6. Addictions

Woman who smoke cigarettes or who abuse cocaine are at increased risk of preterm labour (Berns 2002).

7. Occupational Factors

Those involved in manual work are more prone for preterm labour.

PREDISPOSING FACTORS

1.**Stress**

Careers which involve considerable physical work and psychological stress are associated with increased preterm births (Papiernik & Kaninski 1974). Prolonged standing decreases uteroplacental blood flow and increases the frequency of large placental infarcts causing growth retardation.

Preterm birth is increased in women living alone, and those who are subjected to physical abuse.

2.**Coitus**

Coitus was not found to be associated but increasing numbers of sexual partners increased the risk of recurrent preterm delivery (Yost NP et al 2006).

3.**Reproductive History**

a. Previous preterm birth

The history of one previous preterm birth is associated with a recurrence risk of 16-41% (Williams 22nd edition), risk increasing with the number of preterm birth and decreasing with the number of term deliveries.

b. Previous abortion

There is increase in the preterm deliveries in woman who experienced one or more second trimester abortions.

c. Cervical incompetence

d. Uterine anomalies

e. Pregnancy Complications

- Multiple pregnancies (Goldenberg RL, 2002)
- Hydramnios
- Preclampsia
- Antepartum hemorrhage
- Second trimester bleeding not due to placental causes

4.Interpregnancy interval

A significant increase in preterm birth was observed when the interval between birth and LMP of next pregnancy was less than 3 month.

5.Fetal Gender

The main fetal factor influencing the rate of preterm delivery is fetal sex , with the preponderance of males delivering preterm.

PREDICTION OF PRETERM LABOUR

Risk scoring system

A risk scoring system devised by Papiernik and modified by Creasy and Govik (1980) has been tested in several regions. Women with scores of more than 10 or more are considered to be at high risk for preterm labour.

Scoring systems are based on the factors which increase risk of preterm delivery, the risk is highest with a previous preterm delivery. Bleeding in pregnancy, urinary tract infections, higher order pregnancies, body mass index <20kg /m^2, previous low birth weight babies and stress (family illness, mortality, violence, financial) are associated with preterm delivery. Unfortunately risk scores don't indentify the majority of women who deliver preterm. They are of limited clinical use (Honest H et al 2004) .

Cervical assessment

Asymptomatic cervical dilatation after mid pregnancy has gained attention as a risk factor for preterm delivery.

Levino and associates found that one fourth of the women who cervices were dilated 2 to 3 cm between 26 and 30 weeks delivered before 34 weeks. Papiernik and Colleagues (1987) in, a study of cervical status before 37 weeks found that precocious cervical dilatation increased the risk of preterm labour.

PAPIERNIK RISK SCORING SYSTEM

Points	Socio-economic factors	Previous medical history	Daily habits	Aspects of current pregnancy
1	Two children at home ,Low socio – economic status	Abortions - 1 Less than 1year(yr) since last birth	Works outside	Unusual fatigue
2	Maternal age <20 yrs or >40yrs ,single parent	Abortions - 2	Smokes more than 10 cigarettes per day more than 3 flights of stairs without elevator	Gain of <5g by 32 weeks
3	Very low socio economic status Heights <150 cm Weight <45 kg	Abortions - 3	Heavy or stressful work that is long and tiring. Long daily commuting, extensive travelling	Breech 32 weeks, weight loss, Head engaged at 32 weeks, febrile illness.
4	Maternal age <18 yrs	Pyelonephritis		Bleeding after 12 weeks, short cervix, opened internal os, uterine irritability
5		Uterine anomaly, second trimester abortion, DES exposure ,conebiopsy .		Placentapraevia Hydramnios
6		Preterm delivery, Repeated second trimester abortion.		Twins, abdominal surgical procedure.

Owen and Colleagues (2003) concluded that the value of cervical length to predict preterm birth before 35 weeks is apparent only in women at high risk for preterm birth.

Richly and Colleagues (1995) used transperineal sonography in 100 women with complaints consistent with imminent preterm birth and compared sonographic measurement with those obtained with conventional cervical examination. This has the advantage of avoiding vaginal instrumentation with preterm ruptured membranes and placenta previa.

Ultrasound is a better modality than digital evaluation of cervical length because the upper half of by cervix which cannot be reached digitally can be measured by ultrasonogram.

Transvaginal ultrasound is better than transabdominal because of close proximity of cervix to probe and less distortion by transducer pressure or full bladder.

Fetal breathing movements

Absence of fetal breathing movement on ultrasound performed at the time of admission on women who presented with threatened preterm labour was also found to be accurate test in predicting spontaneous preterm birth .

Uterine activity monitoring

Current opinion is that for most patients home uterine monitoring is not better than frequent nursing contact and support .

Katz and Associates found that women who has subsequent preterm delivery had increased uterine contractions at 30 weeks .

Only patients, who cannot recognize adequately the presence of contractions like multifetal gestation and other overdistended uterus may benefit from home uterine monitoring .

Fibronectins

The presence of fetal fibronectin in cervicovaginal secretions in late second and early third trimester has been proposed as a specific predictor of preterm labour (Lock wood and coworkers 1991).It represents disruption of choriodecidual interface which can be caused by preterm labour. It can be measured using ELISA and values exceeding 50ng/ml are considered positive result. However of concern is the high false positive rate if there is contamination with amniotic fluid, semen, maternal blood and in patients with cerclage. The test is more accurate in predicting spontaneous preterm birth within 7-10 days in women with symptoms of threatened preterm labour before advanced cervical dilatation.

The high negative predictive value of fetal fibronectin can be used to influence management (Honest H et al 2002).

Honest et al found that in **asymptomatic** women ultrasonography measurement of cervical length using cut off of 25mm or less between 20-24 weeks gestation is likely to be accurate in predicting spontaneous preterm birth.

In **symptomatic** women the group found that cervicovaginal fetal fibronectin and absence of fetal breathing movements on ultrasonogram are likely to be accurate in predicting preterm birth

Biochemical markers

1. Salivary oestriol : progesterone ratio
2. Salivary oestriol >1.8/ml before 34 weeks has a sensitivity of 68% and specificity of 76% for preterm labour before 35 weeks of gestation (Darne et al)
3. Serum collagenase
4. Tissue inhibitor of metalloproteinase (TIMP) / Matrix Metalloproteinases
5. Relaxin
6. Corticotrophin Releasing Hormone (CRH)
7. Human chorionic gonadotropin

8. Mediators of inflammation and infection
    a. C-Reactive protein
    b. Granulocyte elastase
    c. Cytokines (IL-6,TNF)
    d. Amniotic fluid glucose concentration
    e. Zinc
    f. Lipocortin -1 (Romeo R et al)
    g. Positive cultures
    h. Granulocyte colony stimulating factor

These are not practically helpful in prediction of preterm labour

DIAGNOSIS OF PRETERM LABOUR

Symptoms of preterm labour

- ❖ Menstrual like cramps
- ❖ Low, dull back ache
- ❖ Pressure (Feels like baby is pushing down)
- ❖ Abdominal cramping
- ❖ Increase or change in vaginal discharge
- ❖ Uterine contractions that are 10 minutes apart or closer

Cunningham GH and coworkers (2001) found that preterm labour is considered to be established if regular uterine contractions can be documented

at least 4 in 20 minutes or 8 in 60 minutes with progressive change in cervical score with effacement 80% or more and dilatation more than 1cm. Contraction are 5 to 8 minutes apart.

If there is absence of cervical change in the presence of contractions the condition is Threatened Preterm Labour .

2**) Pelvic examination**

3) Ultrasongogram

Ultrasonographic assessment in preterm labour

- Fetal viability
- Gestational age
- Estimated fetal weight
- Indicators of preterm labour
    - Transvaginal cervical assessment
    - Fetal breathing movements
- Amniotic fluid volume
- Number of fetus
- Fetal presentation and lie
- Fetal movements and tone
- Fetal anomaly
- Placental localisation and morphology
- Uterine fibroid and adnexal mass

4.Tococardiography

The amplitude, duration, shapes of contraction frequency and basal tone and monitored. The uterine activity is monitored .

Changes in FHR(Fetal Heart Rate) pattern occurring in preterm labour is normally due to immaturity of cardiovascular system. Repetitive late decelerations, absent variability and variable decelerations are sign of placental insufficiency.

PREVENTION OF PRETERM LABOUR

I Basic care

1. Support system of family and friends should be developed.
2. Numerous suggestions on coping with physical and mental stresses of maintaining a pregnancy should be described.
3. Education, supportive services from health care providers and financial issues are of common concern.

4. Behavioural and lifestyle modification
    a. Smoking cessation (Burguet et al)
    b. Avoidance of illicit drugs
    c. Adequate nutrition.

II Bedrest and Hydration

Although bedrest and hydration are widely used as the first step of prevention and treatment, there is no evidence that this practice is beneficial (Freda MC et al, Goldenberg RL et al.,).

Bed rest should be advised with caution after evaluating its benefits and risks in an individual, and not routinely keeping in mind its adverse effects like venous thrombosis and pulmonary edema.

Aggressive treatment of cervicovaginal infection

Bacterial vaginosis has been consistently associated with a 1.5 to 3 times increased risk of spontaneous preterm birth. But the efficacy of treatment in reduction of preterm births is conflicting (Goldenberg R, et al) 1998). But recent systematic review by Varma R, Gupta JK 2006 concluded that screening and treatment of asymptomatic bacteruria and bacterial vaginosis in low risk population groups may reduce the rate of preterm deliveries.

Most Randomised control trials show that intravaginal clindamycin cream used to treat bacterial vaginosis does not prevent preterm birth. (Kekki et al, 2001).

A Cochrane metaanalysis by King & Flenady (2003) of 10 randomized control trials found no difference in the rates of newborn respiratory distress syndrome or of sepsis between placebo and antimicrobial treated group, but did find an increase in perinatal morbidity in the antimicrobial treated group. Presence of GBS (Group B Streptococcus) colonisation in pregnancy has not been found to increase the rate of preterm delivery (Daskalakis G et al 2006).

Cervical Encerclage

A short cervix diagnosed by ultrasound in asymptomatic women may be an indication for cerclage. The role of cervical cerclage for the prevention of preterm delivery is now disputed. A number of systematic reviews which demonstrate a trend towards reduction in preterm deliveres before 34 weeks in high risk women who had cerclage compared to those managed expectantly (Honest H, et al).

Two randomized trials by Lazar et al., and Rush et al., did not show benefit for routine cerclage in women at moderate risk of preterm labour. Also cerclage has an inherent risk which actually increase preterm labour by increasing the pericervical inflammation or infection. Hence unless the diagnosis is specific it is not recommended.

But a MRC/ RCOG trial in low risk women demonstrated that cerclage was associated with low risk of delivery below 33 wks.

Progesterone

Weekly intramuscular administration to women at high risk for preterm labour resulted in lower rates of preterm birth and perinatal mortality when compared with that of placebo, Meis and collaboraters (2003).The dose used by Meis et al was 250 mg of 17 hydroxy progesterone caproate, intramuscularly every week from 20 to 36 weeks.

In addition, da Fonseca and Colleges 2003 reported the effectiveness of a 100mg vaginal suppository of natural progesterone to reduce preterm delivery in high risk women.

A Cochrane Systematic Review in 2006 by Dodd JM et al found that the use of progesterone in women with history of spontaneous preterm birth resulted in a reduction in risk of preterm birth before 34 weeks of gestation and Infant birth weight less than 2500 grams. But the dose, route of administration and time for commencement of therapy has not been arrived conclusively by the study for need of further information. For women with threatened preterm labour the role of progesterone is uncertain as per this review.

MANAGEMENT OF PRETERM LABOUR

Bedrest and hydration

Steroids

In 1995, a National Institute of Health Consensus Development Panel recommended corticosteroids for fetal lung maturation in preterm labour.Since then there has been nearly universal acceptance and implementation of these recommendations.

All pregnant women between 24 and 34 weeks of gestation who are at risk of preterm delivery within 7 days should be considered candidates for antenatal corticosteroids.

Recommended regimens includes a single course of two doses of 12 mg of betamethasone given intramuscularly 24 hours apart,or four doses of 6mg of dexamethasone given intramuscularly 12 hours apart.

A Cochrane Systematic Review by Rober D, Dalziel SR 2006 found that antenatal corticosteroids reduce neonatal death, respiratory distress syndrome, intraventricular hemorrhage. Also antenatal corticosteroid is not associated with changes in the rates of maternal death, maternal infection, fetal death, neonatal chronic lung disease or birth weight. It is also associated with a reduction in incidence of necrotising enterocolitis and

systemic infections in the first 48 hours of life as well as reduction in the need for respiratory support or neonatal intensive care unit admission.

Although benefit on neonatal outcome is maximum between 24 hours and 7 days after initiation of therapy, steroids confer significant survival advantages even when delivery occurs within 24 hours .Therefore treatment should not be withheld when delivery is probable within 24 hours.

Tocolysis

Tocolysis is pharmacological suppression of uterine activity.

Indication:

Preterm delivery is a major cause of perinatal morbidity and mortality.Tocolytic agents are effective in reducing the likelihood of delivery within 48 hours but do not reduce the overall risk of preterm delivery.

Consideration should be given for administration of tocolytics to all women experiencing preterm labour when there is a delay in delivery

- to permit in-utero transfer to a tertiary perinatal centre for multi disciplinary management (obstetrician, neonatologist, anaesthetist); and /or
- to gain upto 48 hours to allow for the administration of corticosteroids to enhance pulmonary maturity.

BETA SYMPATHOMIMETICS

Caritis et al 1976, noted that small doses of epinephrine inhibited uterine hyperactivity. Efforts to produce an epinephrine like compound which lacked the cardiovascular stimulant effect culminated in the synthesis of β agonists.

I generation: - Isoxsuprine, Orciprenaline, isoprenaline

II generation: - Ritodrine, Terbutaline, Fenoterol

The most commonly used β2 agonist for tocolysis is ritodrine; then are terbutaline and salbutamol.

Ritodrine :-

Ritodrine infusion is started at a dose of 50μg /min and increased very 20 minutes until uterus is quiescent or side effects limit escalation of dose.

Side effects are palpitations, tremor, nausea, headache, chest pain, dyspnoea, pulmonary edema, hypokalemia, myocardial ischaemia, arrhythmias.

Terbulaline:-

Not used as much as ritodrine, but is effective in temporarily suppressing contraction when given parenterally.

Intravenous dose is 5-10μg /min, increased every 10-15 min to a maximum of 80 μg. 2.5 -5mg is given orally every 4-6 hours & 250μg subcutaneously every 20-30 min ,given as 4-6 doses. Terbutaline has higher a risk of hyperglycemia than ritodrine. Other side effects are similar. But β2 agonists are no longer the first choice of drugs for tocolysis because of their side effects (RCOG Clinical Guide lines,2002 and Anotayanonth et al., 2004).

Contraindications of β2 agonist:-

- Symptomatic cardiac disease especially ventricular outflow obstruction.
- Conduction disturbance.
- Hyperthyroidism.
- Sickle cell disease.
- Uncontrolled maternal diabetes mellitus.
- Chorioamnionitis.
- Eclampsia or severe preeclampsia.
- Multifetal gestation.
- Severe obstetrical bleeding

MAGNESIUM SULPHATE

$MgSO_4$ uncouples the depolarisation contraction coupling. During the depolarisation of myometrial cells, Mg^{++} competes with Ca^{+} for entry into the cell causing less intracellular Ca^{2+} to participate in actin-myosin interaction during smooth muscle contraction. It affects neural transmission by modifying acetyl choline release and sensitivity at motor end plate.

Contractility is inhibited at serum level of 5-8mEq/dl. Deep tendon reflexes are lost at 9-13mEq/dl. Respiratory depression occurs at > 14mEq/dl.

Dosage

Intravenous loading dose of 4g administered over 20 minutes followed by maintenance dose of 1-2g/hr.

Side effects include flushing, dizziness, nausea, lethargy, chest tightness, hypocalcemia, pulmonary edema, respiratory depression and depressed motor, respiratory activity in fetus. It is contraindicated in myasthenia gravis, heart block, renal disease, recent myocardial infarction.

Magnesium sulphate is an ineffective tocolytic agent as shown by a Cochrane systematic review(Crowther et al, 2002; Cox etal 1990).

PROSTAGLANDIN SYNTHETASE INHIBITORS

Drugs like aspirin, indomethacin, naproxen fenamate and sulindac inhibit the prostaglandin synthesis , decrease the myometrial gap junctions and decrease the influx of calcium.

Maternal side effects includes nausea, vomiting, drug rash, headache, gastritis, diarrhoea. In fetus it produces constriction of ductus arteriosus, pulmonary hypertension and oligohydramnios. Intraventricular hemorrhage, necrotising enterocolitis have also been reported.

They are effective as single dose in inhibiting the myometrial activity in many women at term (Reiss et al, 1997). Two randomised trials which compared the effect of indomethacin and placebo in delaying delivery showed significant delay at 48 hours and at 7-10 days.

Comparison with agonists show similar efficacy, but a better side effect profile (RCOG guideline 2002). However,their use is limited because of their effects on the fetus.

CALCIUM CHANNEL BLOCKERS

They are heterogenous group of organic compounds that inhibit the influx of extracellular calcium across the cell membrane during inward calcium current of action potential.They block the voltage sensitive L Type

of calcium channels. They also inhibit the release of intracellular calcium from the sarcoplasmic reticulum. Thus they reduce the tone of smooth muscles.

The commonly used drug Nifedipine is a potent inhibitor of myometrial contractions in non pregnant, pregnant and post partum uterus (Anderson et al, 1979).

Treatment Regime

The optimal dosing regime of Nifedipine has not yet defined. Read and Wellby 1986, George et al 1991, showed that an initial dose of 30mg followed by 20mg 8th hourly for 3 days, reported a 75% successful tocolysis in 71% and 76% respectively. The tocolytic regimen given in Obstetrics and Gynaecology Clinics of North America (Andrienne Z et al) is loading dose 30 mg orally and maintenance dose of 10-20 mg orally every 4-6 hrs.

In Clinical Obstetrics and Gynaecology 2000, Amy E et al found the following dosing regimens in various study protocols. Most administered a initial loading dose of 30mg of oral nifedipine followed by 10mg to 20mg dose every 4 to 6 hrs .Sublingual nifedipine loading doses are no longer advised.

Onset of action after oral nifedipine is less than 20 minutes with peak plasma concentration in 1 hour (range 15-90 min) and half life of 1.5 to 3 hrs. Duration of action of a single dose can be as long as 6 hrs but no apparent cumulative effect occurs when administered orally every 6 hour. Elimination is mainly through kidneys (70%) and bowels 30% (Amy et al).

Nifedipine has been compared to beta agonists in several randomised studies which suggest that calcium channel blockers are more effective, better tolerated with fewer side effects and have lower neonatal morbidity.

Side effects include facial flushing, nausea, headache, hypotension and tachycardia. There is no significant alteration in serum electrolytes and blood glucose.

Mari et al, (1989) found that short term nifedipine does not adversely affect uteroplacental and fetal blood flow when evaluated by doppler at doses used for preterm labour.

OXYTOCIN ANTAGONISTS (ATOSIBAN)

There will be increase in myometrial oxytocin receptors in labour. The analogue competitively blocks the oxytocin receptors and inhibits preterm labour.

Atosiban is given intravenously 6.75mg bolus over one minute followed by infusion at 18mg/hr for 3 hours and then 6mg/hr for upto 45 hours. Duration of treatment should not exceed 48 hrs and the total dose should not exceed 330mg of atosiban. Side effects are nausea, chest pain, vomiting and dyspnoea. Compared to β agonist atosiban has similar efficacy but a better side effect profile.

Royal College of Obstetricians and Gynaecologists guidelines 2002, suggest that if tocolytics are administered, the first choice should be oxytocin antagonists or Nifedipine.

But compared with other tocolytics atosiban therapy is costly.

NITRIC OXIDE DONORS (GLYCERYL TRINITRATE)

Nitiric oxide is a potent endogenous hormone causing smooth muscle relaxation.

The NO donors inhibit corticotrophin releasing hormone secretion which acts as a promoter of parturition.

10mg of Glyceryl Trinitrate patch is applied over the fundal region of maternal abdomen. If tocolysis is not achieved in one hour, another 10mg patch can be applied to a maximum dose of 20mg in 24 hours .Cochrane review (2000)by Duckitt K et al showed that nitroglycerine did

not delay delivery or improve neonatal outcome when compared with placebo, no treatment or alternative tocolytics.

K+ CHANNEL OPENERS:

Diazoxide is a medication structurally related to the thiazide diuretics that is used in treatment of hypertensive crisis. It inhibits contractility of smooth muscles, there by rendering myometrial quiescence.

Dosage is 5mg /kg, given intravenously slowly in 15-30 minutes. The drug is diluted in half normal saline. It can also be given in boluses of 50-100mg every 5 minutes.

Side effects are hypotension, tachycardia, hyperglycemia, and decreased uteroplacental blood flow secondary to maternal hypotension. The fetal side effects are hypoglycemia and fetal distress secondary to maternal hypotension. Further evaluation of this newer group of tocolytic drugs is needed.

AIM OF THE STUDY

AIMS OF THE STUDY

1. To study the efficacy of Nifedipine in prolonging the pregnancy in preterm labour.
2. To record the effects of Nifedipine in the mother and the fetus.

MATERIALS AND METHODS

MATERIALS AND METHODS

Study design

It is a prospective study conducted in Government RSRM Lying in Hospital attached to Stanley Medical College, Royapuram from September 2008 to September 2009. The study population comprised of patients who attended either the hospital outpatient department or causality. There were 100 patients in Nifedipine group and 10 patients were lost to follow up. 100 cases were taken as controls of whom 13 cases were lost to follow up. Study group received nifedipine and control group were observed with bed rest. Both the groups received intramuscular corticosteroids. In view of the ethical issue, written informed consent was obtained.

Inclusion criteria

1. Gestational age (GA)between 28 to 34 weesks as determined by menstrual dates, clinical examination, Ultrasonogram (USG) Abdomen
2. Uterine contractions. 4 contractions in 20 minute period lasting for 40 -45 seconds
3. Progressive cervical effacement upto 75%
4. Cervical dilatation upto 3 cm
5. Intact membranes

Exclusion criteria

Maternal conditions

1. Rupture of Membranes
2. Infection
3. Cervical dilatation greater than 3 cm
4. Antepartum hemorrhage
5. Polyhydramnios/Oligohydramnios
6. Pregnancy induced hypertension(PIH)
7. Chronic hypertension
8. Cardiac disease
9. Previous caesarean section
10. Renal disease
11. Pulmonary disorder –Asthmatics, ARDS (Adult Respiratory Distress Syndrome)
12. Uncontrolled maternal diabetes mellitus.

Fetal factors

1. Multiple gestation
2. Fetal death / distress
3. IUGR(Intrauterine Growth Restriction)
4. Congenital anomalies
5. Erythroblastosis fetalis

Investigations

1. Urine analysis
2. Complete blood count
3. Vaginal swab
4. ECG (Electrocardiogram)
5. USG Abdomen

Drug protocol

On admission, patients were put in left lateral position. BP (Blood Pressure), PR (pulse rate) recorded. Cardiovascular System (CVS), Respiratory System (RS) examined. Steroids given.

Group A

Cap. Nifedipine 10mg was given orally. If uterine contractions persisted after 20 minutes, the dose was repeated every 20 minutes, upto a maximum total dose of 30mg during first hour of treatment. If oral nifedipine suppressed uterine activity, then maintenance therapy of 10mg 6^{th} hourly of oral nifedipine initiated 3 hrs after the last oral dose. This was continued for 3 days.

If uterine contractions did not cease within 1 ½ hours, patient was deemed a failure and treatment stopped. Treatment considered successful if

there was abolition of uterine contractions and no progress of cervical dilatation and postponement of labour for atleast 48 hours.

Group B

Observed with bed rest.

Both the groups receive intramuscular corticosteroids.

The variables monitored

1. BP ,PR,Temperature,RR hourly during both phases.
2. Systolic BP<100mm Hg or PR >100 or Temperature >37.5 C will be reported.
3. Careful watch for side effects.
4. If initial cardiotocograph is reactive, FHR (fetal heart rate) will be recorded hourly during stabilization phases and thereafter four hourly for first 48 hours.

Definition of success (S)

Several factors have been considered for assessing the success of tocolysis by various authors.

In this study successful tocolysis was defined as the delay of delivery with suppression of contractions for more than 48 hours form the initiation of therapy.

Definition of Failure (F)

The therapy was said to have failed when the patient delivered within 48 hours of initiation of therapy, and tocolysis was stopped when cervical dilation progressed to >3cms or when the membranes ruptured spontaneously.

Hence this study confines itself to the study of idiopathic spontaneous preterm labour, comparing the efficacy of nifedipine with that of control in prolonging pregnancy for atleast 48 hours and studying the maternal and fetal effects.

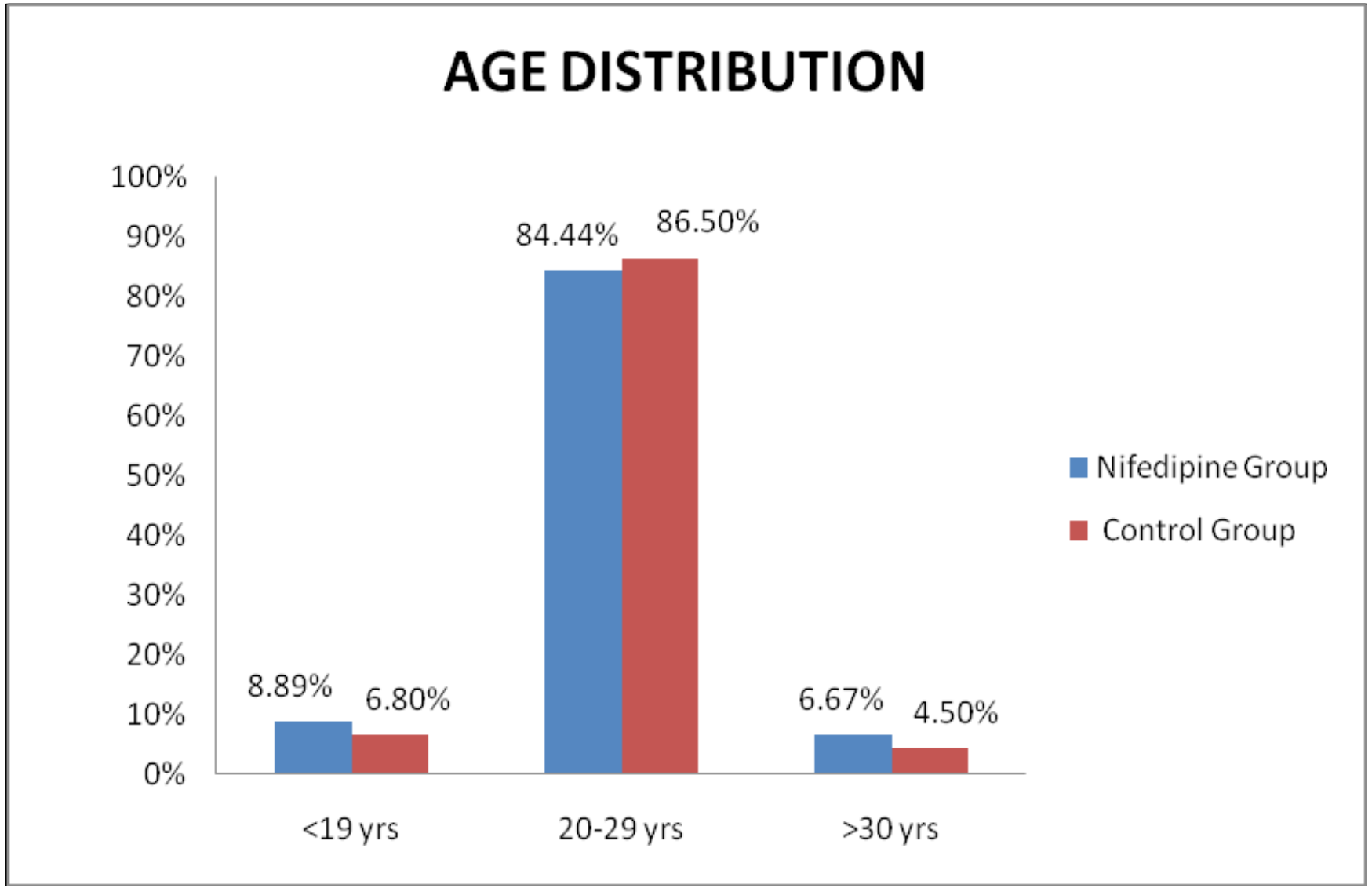
RESULTS AND OBSERVATION

AGE DISTRIBUTION

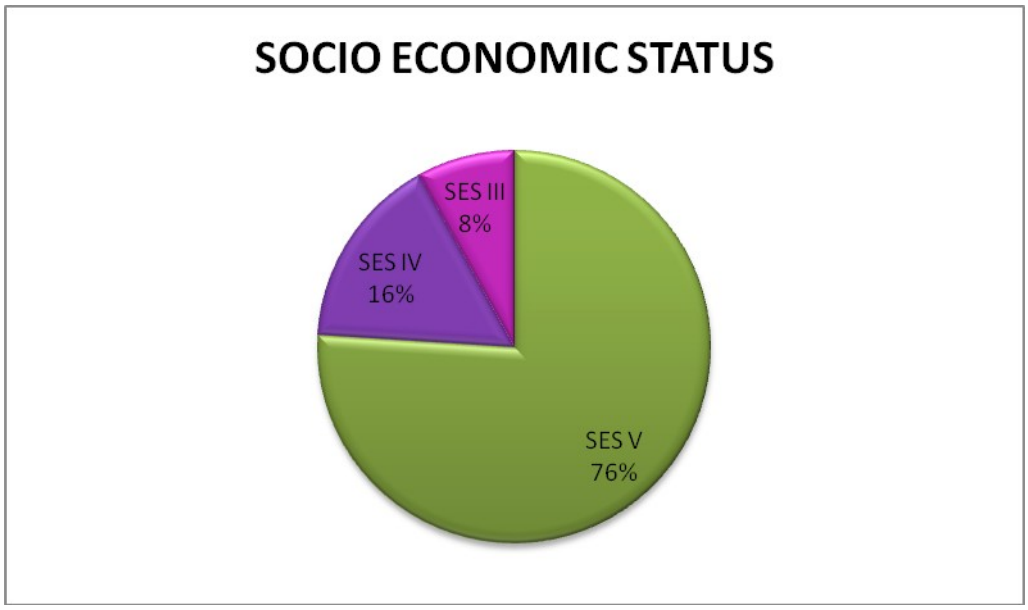
Table :1

Age in years	Nifedipine Group		Control Group	
	No.	%	No.	%
<19	10	8.89%	6	6.80%
20-29	44	84.44%	77	88.5%
>30	36	6.67%	4	4.5%

Maximum incidence of preterm delivery was observed in the 20-29 years against the usual consensus that highest incidence occurs in <19 and >30years. This may be due to increased age at marriage and increased awareness of pregnancy complications in that age group.


AGE DISTRIBUTION
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
8.89%
6.80%
84.44%
86.50%
6.67%
4.50%
<19 yrs
20-29 yrs
>30 yrs
Nifedipine Group
Control Group

SOCIO ECONOMIC STATUS



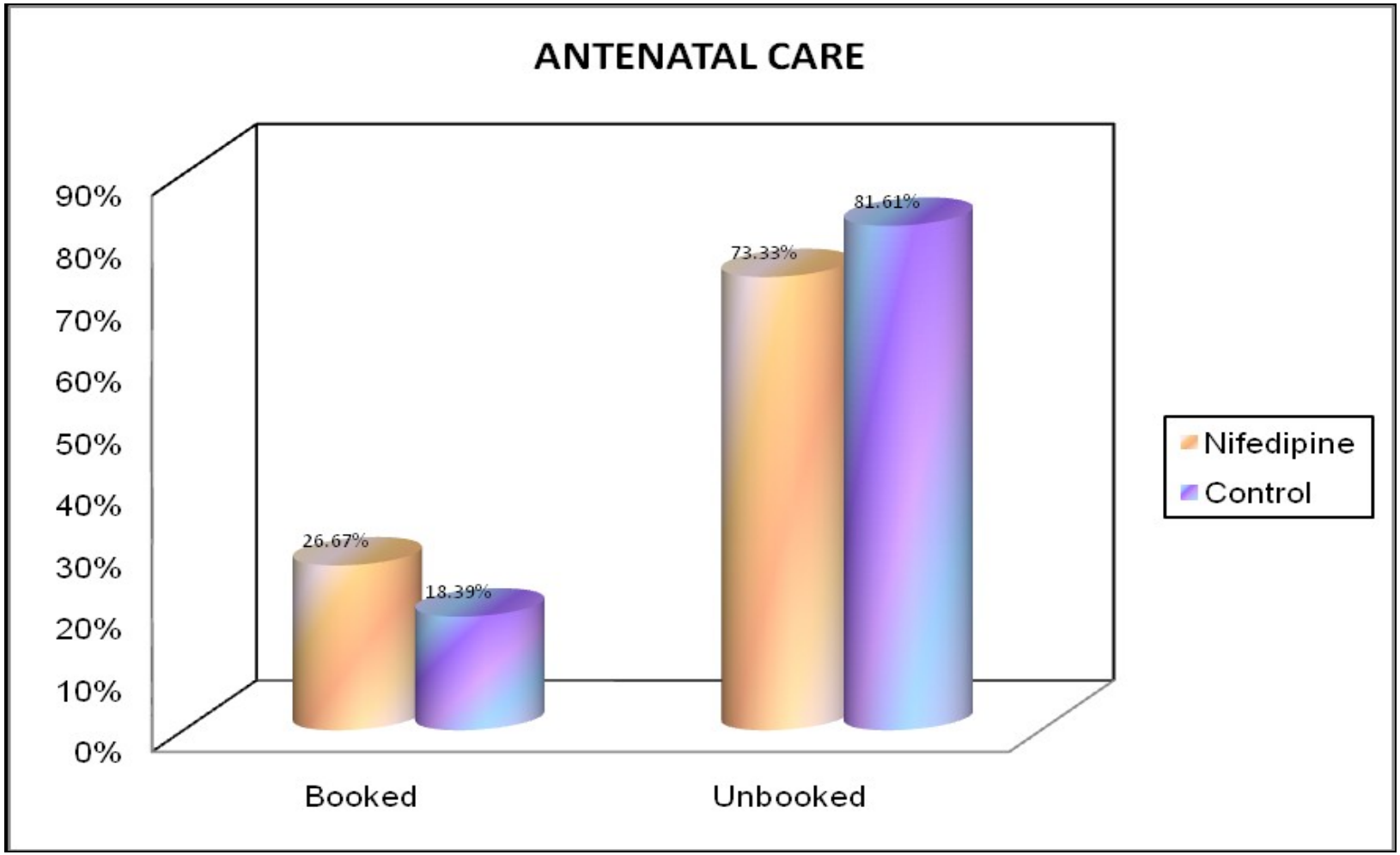
Patient from socio economic status SES V constituted 76% SES IV 16% and SES III 8%. Preterm labour is common in low socioeconomic and nutritional status.

ANTENATAL CARE

Table :2

Booked /Unbooked	Nifedipine Group		Control Group	
	No.	%	No.	%
Booked	24	26.67%	16	18.39%
Unbooked	66	73.33%	71	81.61%

Preterm labour was more common among unbooked patients while the booked patients who had atleast 3 visits were educated about preterm labour and its complications. Regular antenatal care was received by 26.67% in Nifedipine Group compared to 18.39% in control group .

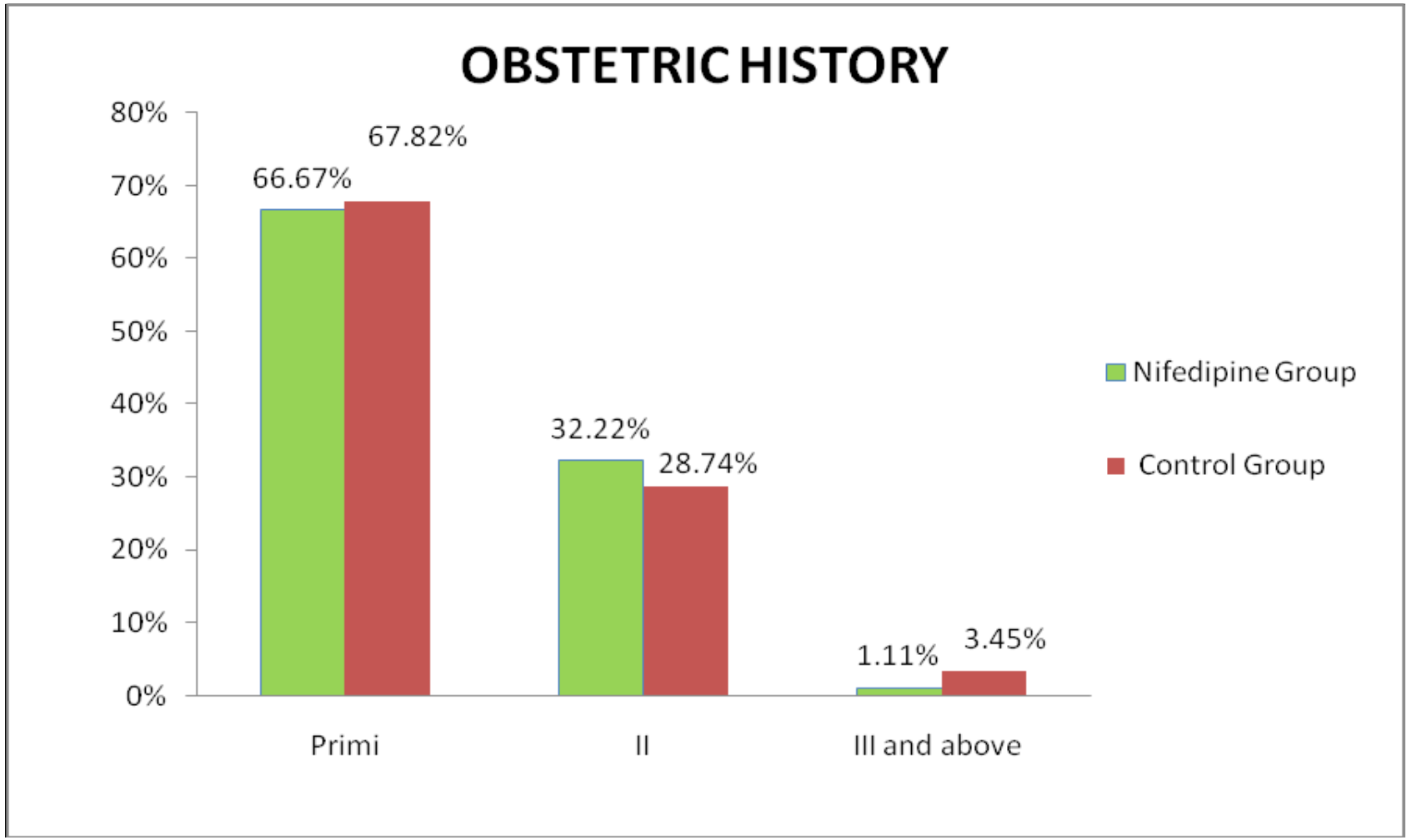

ANTENATAL CARE
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
26.67%
18.39%
73.33%
81.61%
Booked
Unbooked
Nifedipine
Control

OBSTETRIC HISTORY

Table :3

Gravida	Nifedipine Group		Control Group	
	No.	%	No.	%
Primi	60	66.67%	59	67.82%
II	29	32.22%	25	28.74%
III and above	1	1.11%	3	3.45%

66.67% and 67.82% of preterm labour was observed among primi gravida Nifedipine and control groups respectively.

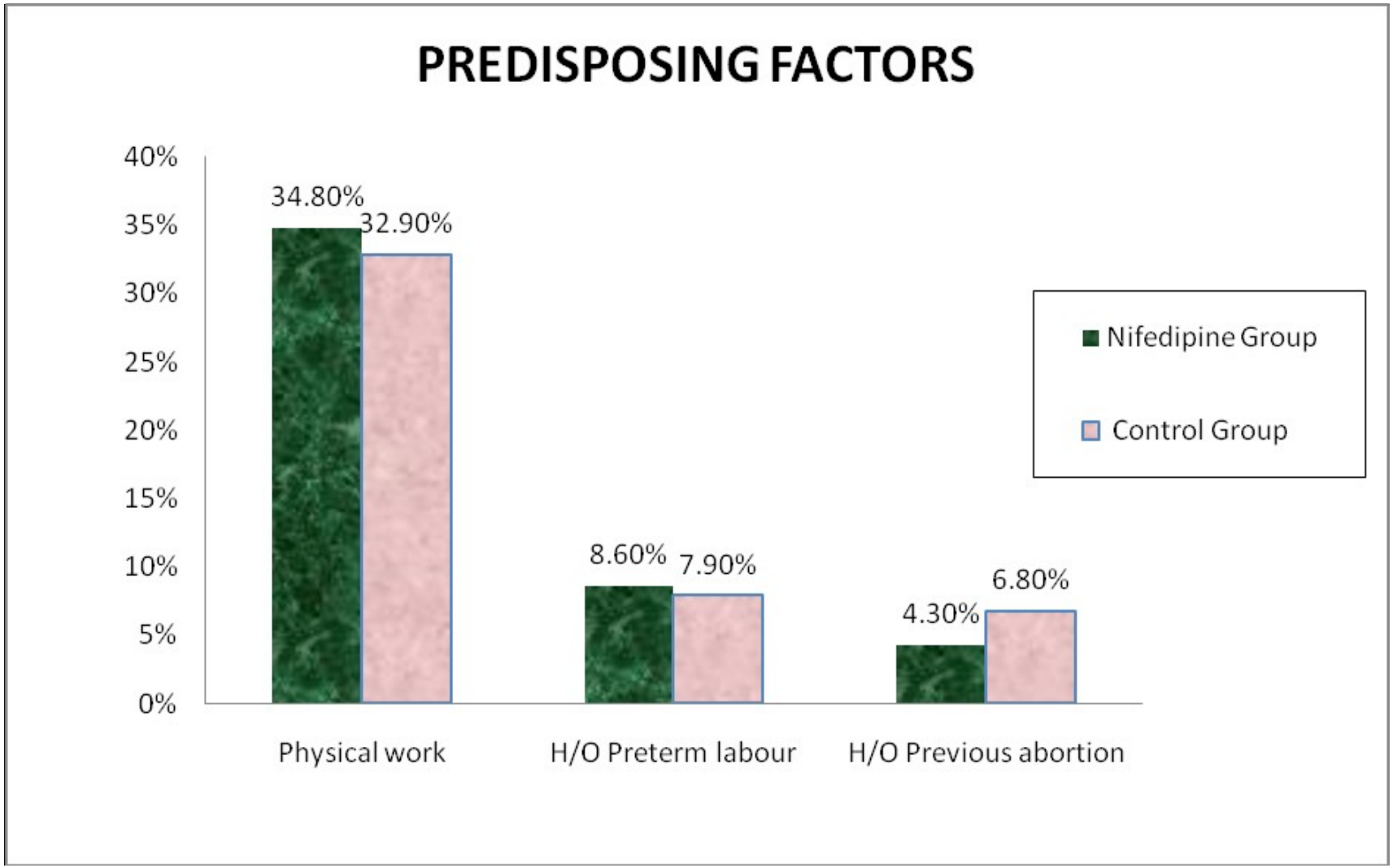

OBSTETRIC HISTORY
80%
70%
60%
50%
40%
30%
20%
10%
0%
66.67%
67.82%
32.22%
28.74%
1.11%
3.45%
Primi
II
III and above
Nifedipine Group
Control Group

PREDISPOSING FACTORS

Table: 4

S.No	Factors	Nifedipine group		Control Group	
		No.	%	No.	%
1.	Physical work	32	34.8%	29	32.9%
2.	H/O Preterm labour	8	8.6%	7	7.9%
3	H/O Previous abortion	4	4.3%	6	6.8%

34.8% and 32.9% had history of excessive physical work, 8.6% and 7.9% had previous preterm delivery, 4.3% and 6.8% had previous one or more abortions in Nifedipine and control groups respectively.

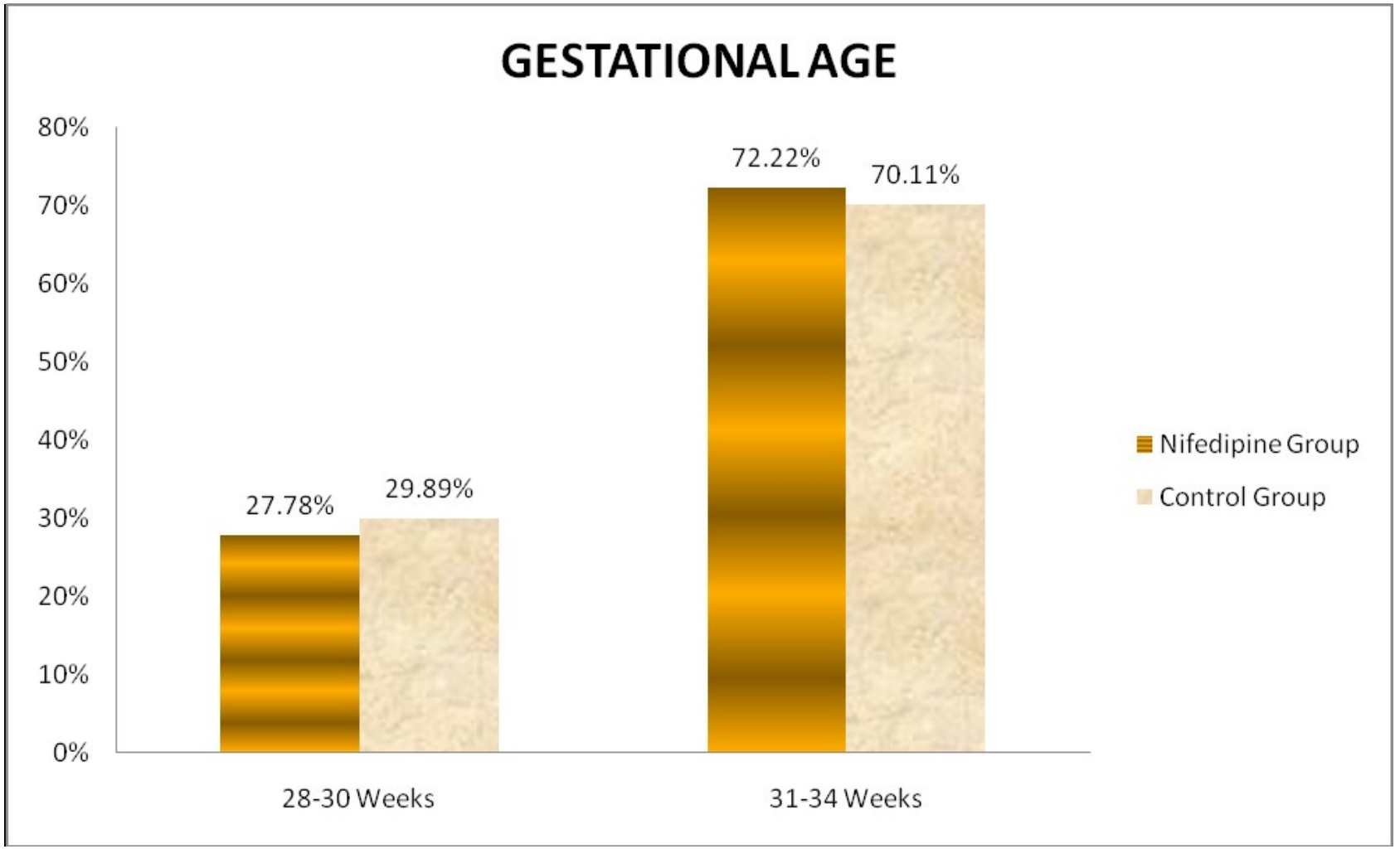

PREDISPOSING FACTORS
40%
35%
30%
25%
20%
15%
10%
5%
0%
34.80%
32.90%
8.60%
7.90%
4.30%
6.80%
Nifedipine Group
Control Group
Physical work
H/O Preterm labour
H/O Previous abortion

GESTATIONAL AGE

Table :5

GA (Weeks)	Nifedipine Group		Control Group	
	No.	%	No.	%
28-30	25	27.78%	26	29.89%
31-34	65	72.22%	61	70.11%

27.78% and 29.89% of preterm labour was observed in gestational age between 28-30 weeks, 72.22% and 70.11% of preterm labour was observed in gestational age between 31-34 weeks in Nifedipine and Control groups respectively.

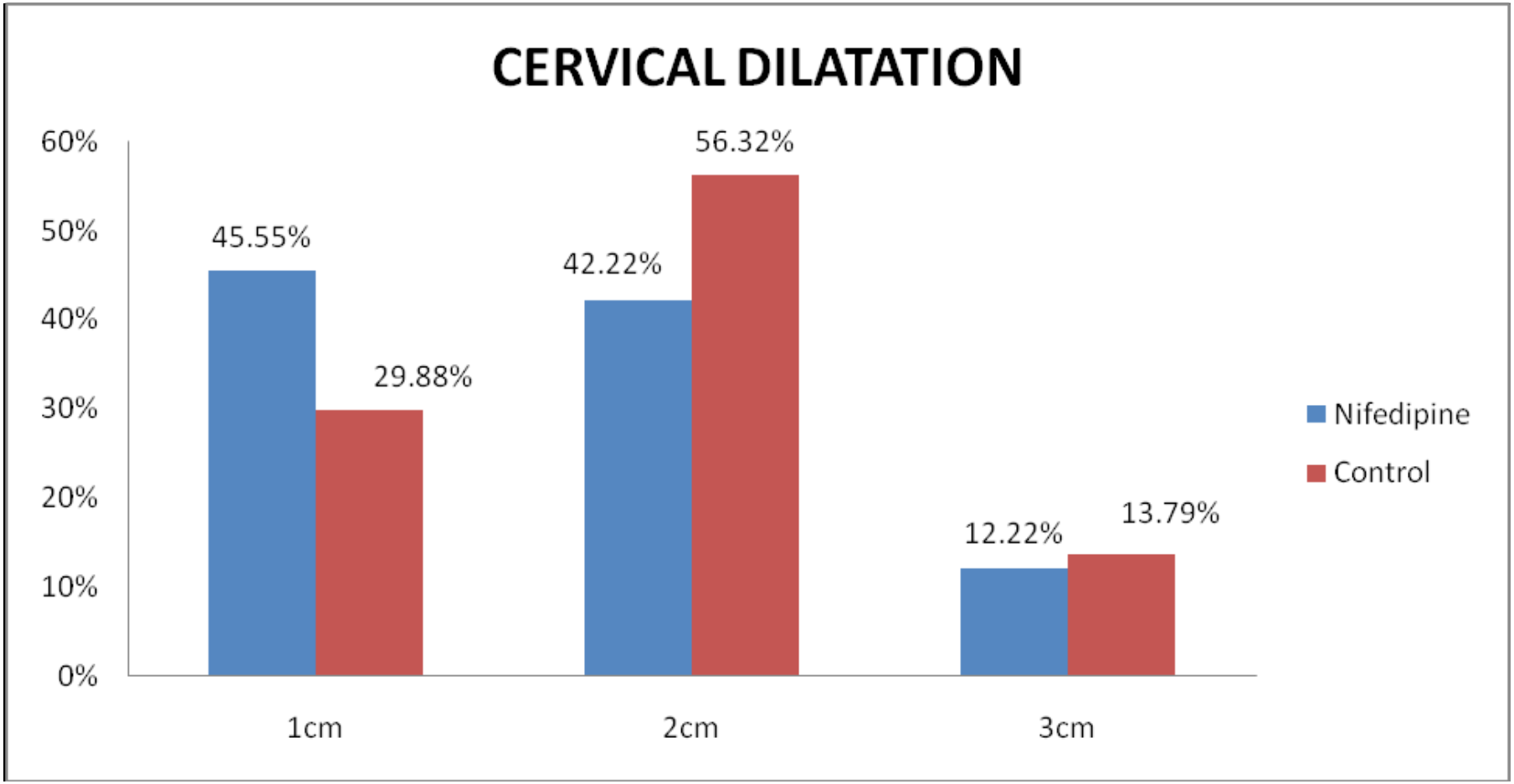

GESTATIONAL AGE
80%
70%
60%
50%
40%
30%
20%
10%
0%
27.78%
29.89%
72.22%
70.11%
28-30 Weeks
31-34 Weeks
Nifedipine Group
Control Group

CERVICAL DILATATION

Table : 6A

P/V Dilation	Nifedipine Group		Control Group	
	No.	%	No.	%
1cm	41	45.55%	26	29.88%
2cm	38	42.22%	49	56.32%
3cm	11	12.22%	12	13.79%

The cervix was 1cm dilated in 45.55% and 29.88%, 2cm dilated in 42.22% and 56.32% and 3cm dilated in 12.22% and 13.79% in nifedipine and control groups respectively.

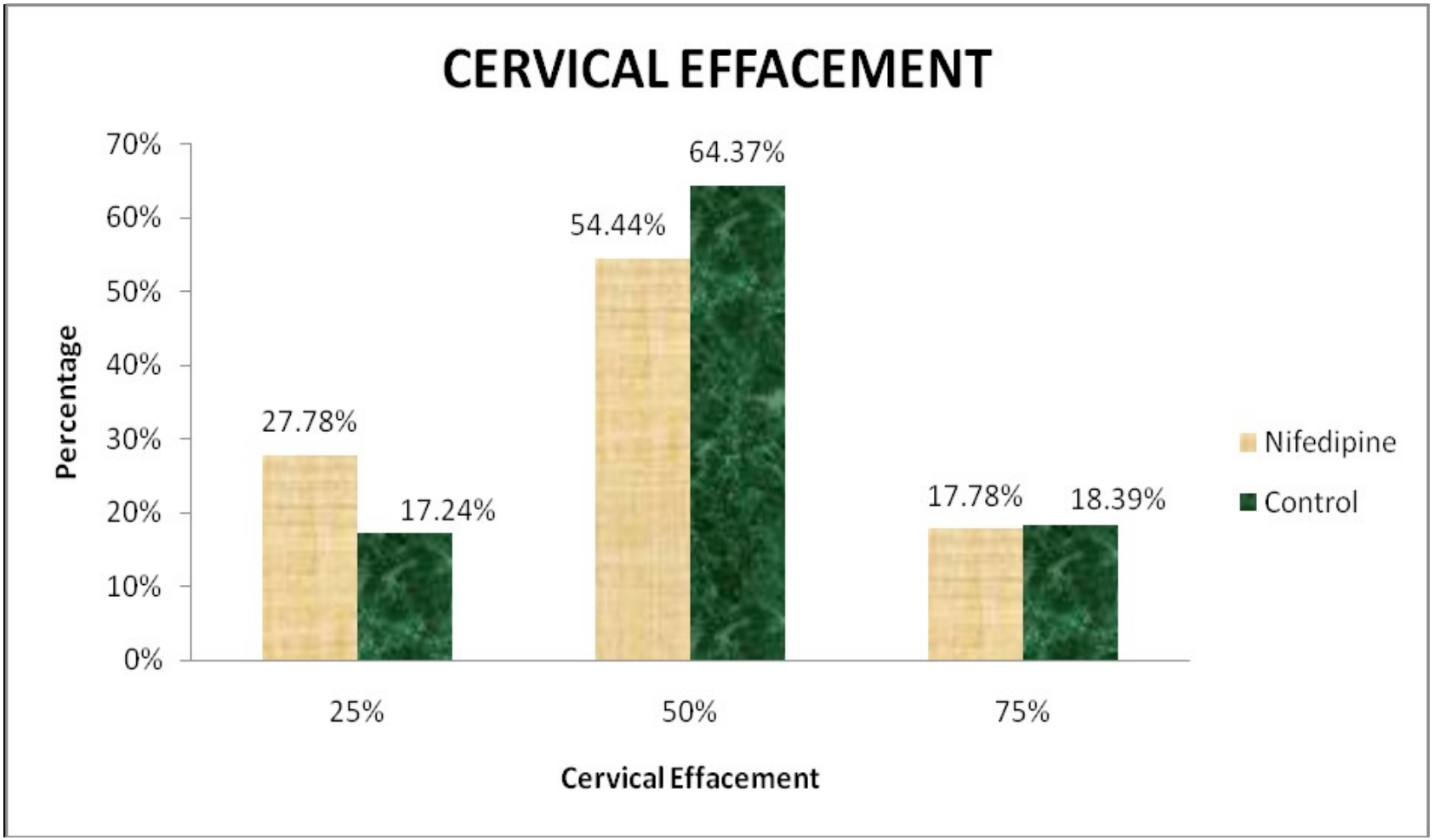

CERVICAL DILATATION
60%
50%
40%
30%
20%
10%
0%
45.55%
29.88%
42.22%
56.32%
12.22%
13.79%
1cm
2cm
3cm
Nifedipine
Control

CERVICAL EFFACEMENT

Table : 6B

P/V Effacement	Nifedipine Group		Control Group	
	No.	%	No.	**%**
25%	25	27.78%	15	17.24%
50%	49	54.44%	56	64.37%
75%	16	17.78%	16	18.39%

The cervix was 25% effaced in 27.78% and 17.24% of cases , 50% effaced in 54.44% and 64.37% of cases and 75% effaced in 17.78% and 18.39% of cases in nifedipine and control group respectively.

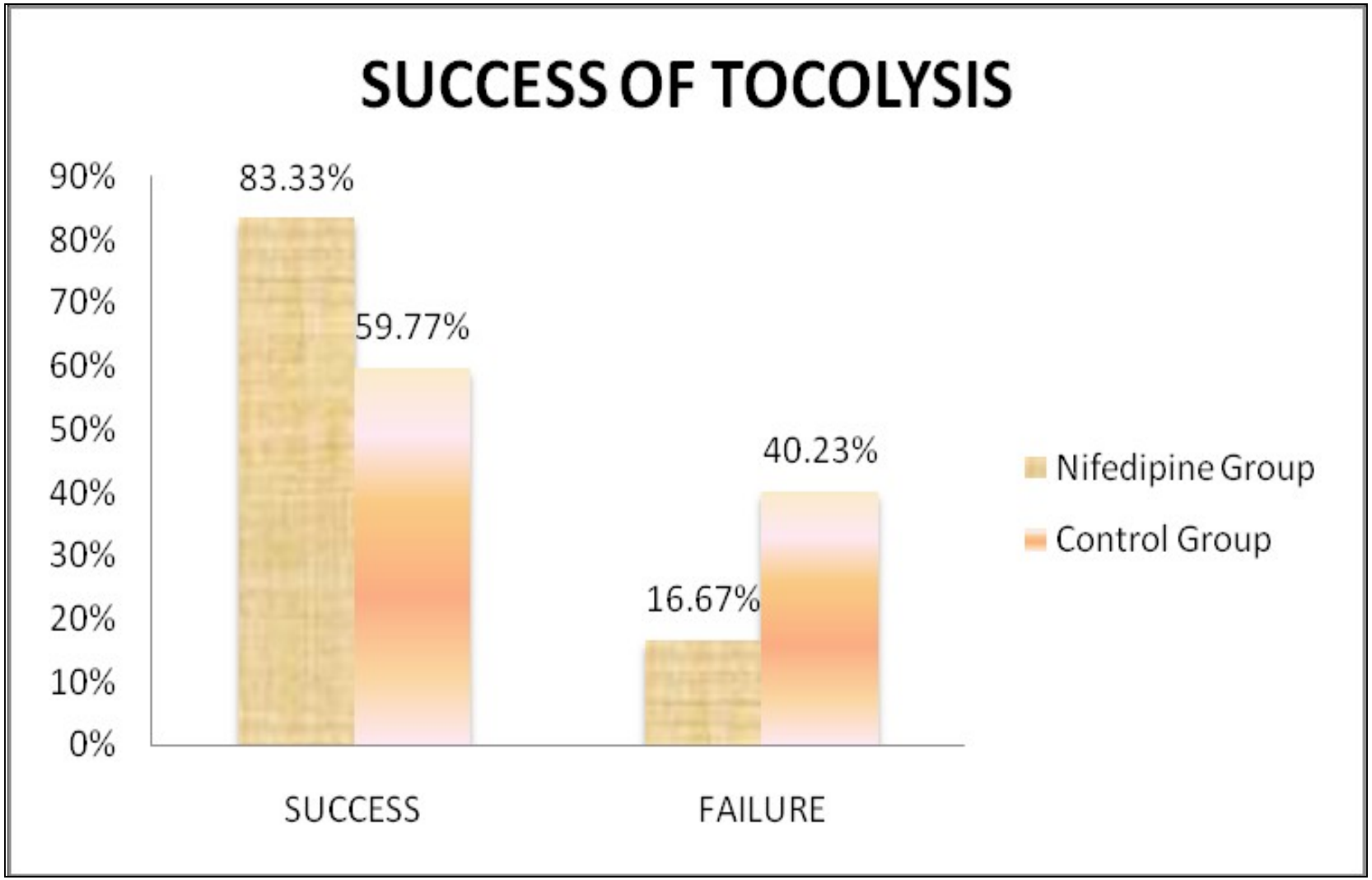

CERVICAL EFFACEMENT
70%
60%
50%
40%
30%
20%
10%
0%
Percentage
27.78%
17.24%
54.44%
64.37%
17.78%
18.39%
25%
50%
75%
Cervical Effacement
Nifedipine
Control

SUCCESS OF TOCOLYSIS

Table :7

Operation S/F	Nifedipine Group		Control Group	
	No.	%	No.	**%**
S	75	83.33%	52	59.77%
F	15	16.67%	35	40.23%

The success in Nifedipine and Controls are 83.33% and 59.77% respectively. By test of proportion, the ‘p’ value was found to be .000 which is statistically significant.

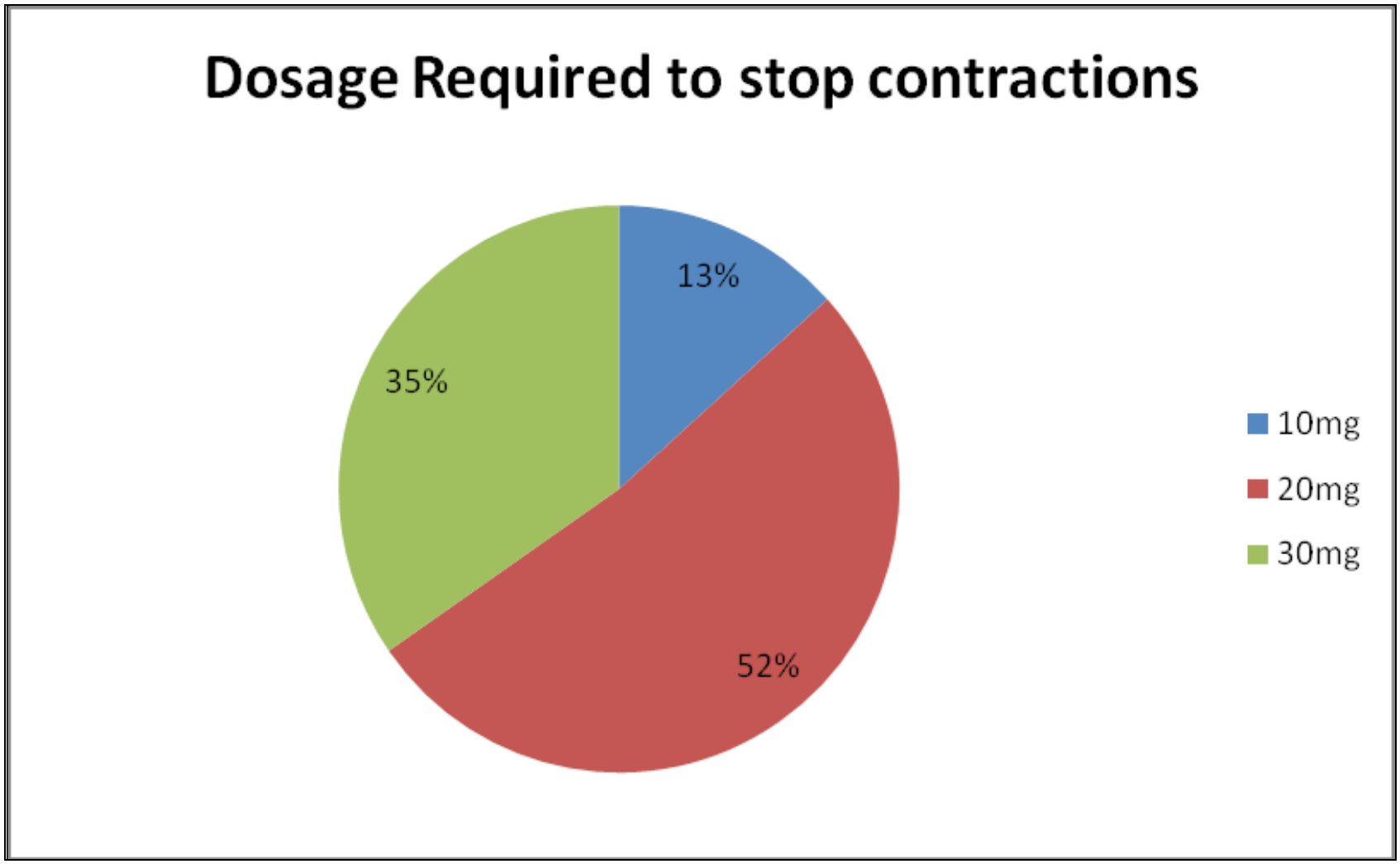

SUCCESS OF TOCOLYSIS
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
83.33%
59.77%
16.67%
40.23%
SUCCESS
FAILURE
Nifedipine Group
Control Group

DOSAGE REQUIRED TO STOP CONTRACTIONS

Table : 8

S.No	Dose of Nifedipine	No.	%
1	10mg	10	13.33%
2	20mg	39	52%
3	30mg	26	34.66%

20 mg of Nifedipine was required to suppress contractions in 52%, 10mg in 13.33% and 30mg in 34.66% of patients in that group.

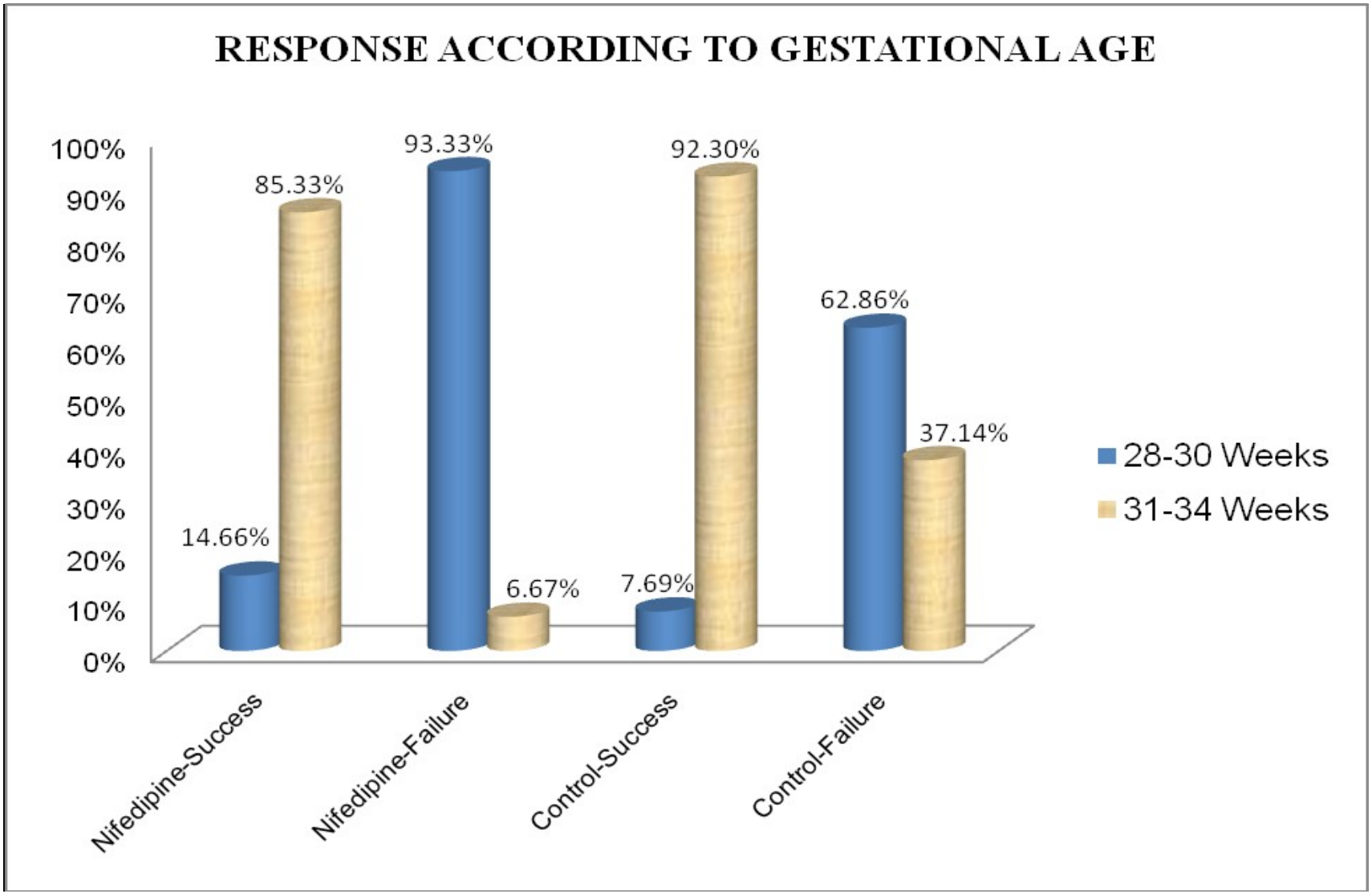

Dosage Required to stop contractions
13%
35%
52%
10mg
20mg
30mg

RESPONSE ACCORDING TO GESTATIONAL AGE

Table: 9

GA (weeks)	Nifedipine				Control			
	Success		Failure		Success		Failure	
	No.	%	No.	%	No.	%	No.	%
28-30	11	14.66%	14	93.33%	4	7.69%	22	62.86%
31-34	64	85.33%	1	6.67%	48	92.30%	13	37.14%

The prolongation of pregnancy more than 48 hours is 92.30% and 85.33% in 31-34 weeks gestational age group, 7.69% and 14.66% in 28-30 weeks gestational age group in control and nifedipine group respectively. P value is .757.

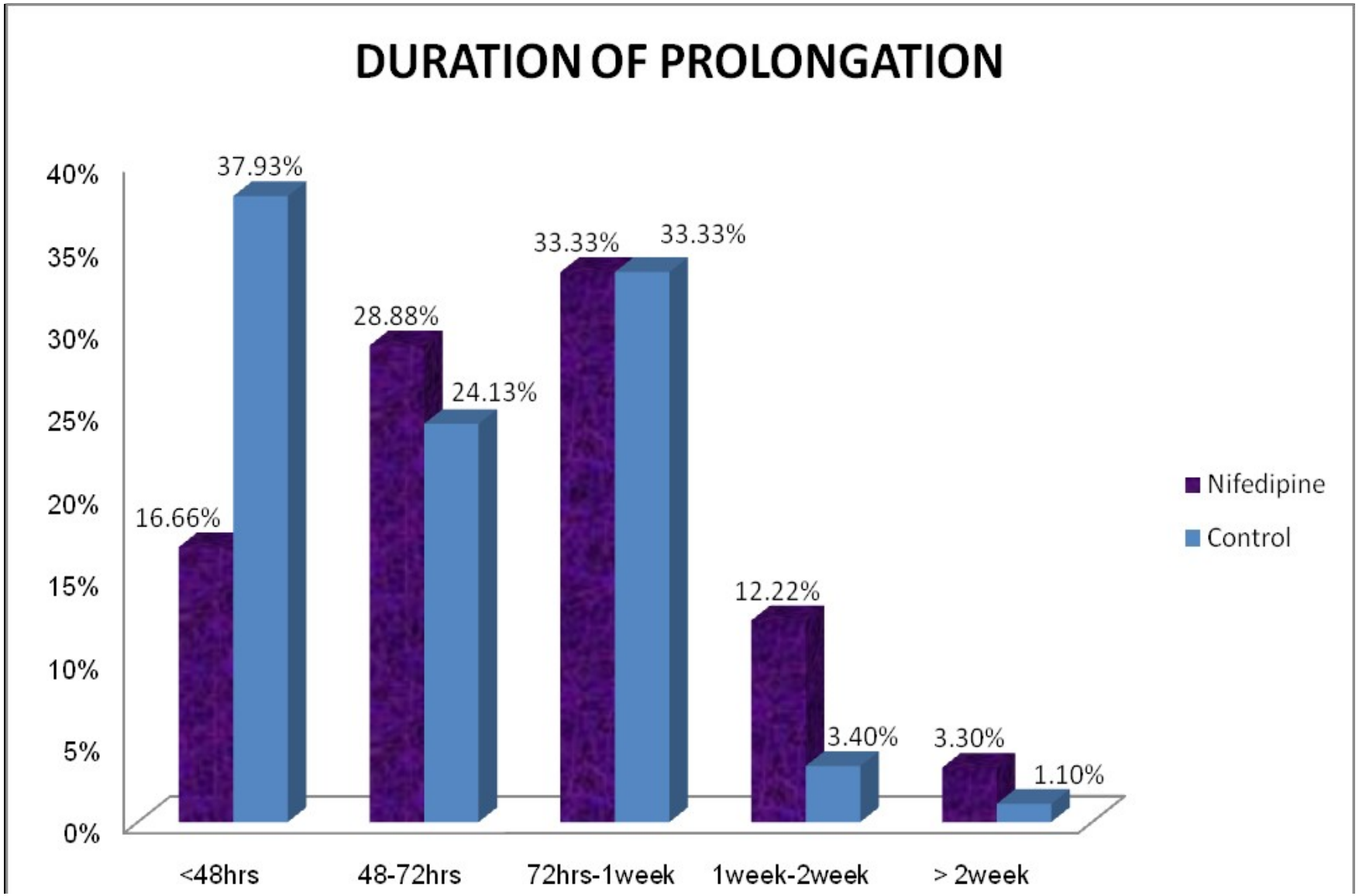

RESPONSE ACCORDING TO GESTATIONAL AGE
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
14.66%
85.33%
93.33%
6.67%
7.69%
92.30%
62.86%
37.14%
Nifedipine-Success
Nifedipine-Failure
Control-Success
Control-Failure
28-30 Weeks
31-34 Weeks

DURATION OF PROLONGATION

Table :10

Prolongation period	Nifedipine		Control	
	No.	Percentage	No.	Percentage
<48hrs	15	16.66%	33	37.93%
48-72hrs	26	28.88%	21	24.13%
72hrs-1week	30	33.33%	29	33.33%
1week-2week	16	12.22%	3	3.4%
> 2week	3	3.3%	1	1.1%

Prolongation beyond 1 week was observed in 15.52% in Nifedipine group 4.5% in control group. Mean duration of prolongation in Nifedipine group was found to be 3.78 days.


DURATION OF PROLONGATION
40%
35%
30%
25%
20%
15%
10%
5%
0%
37.93%
33.33%
33.33%
28.88%
24.13%
16.66%
12.22%
3.40%
3.30%
1.10%
<48hrs
48-72hrs
72hrs-1week
1week-2week
> 2week
Nifedipine
Control

MODE OF DELIVERY

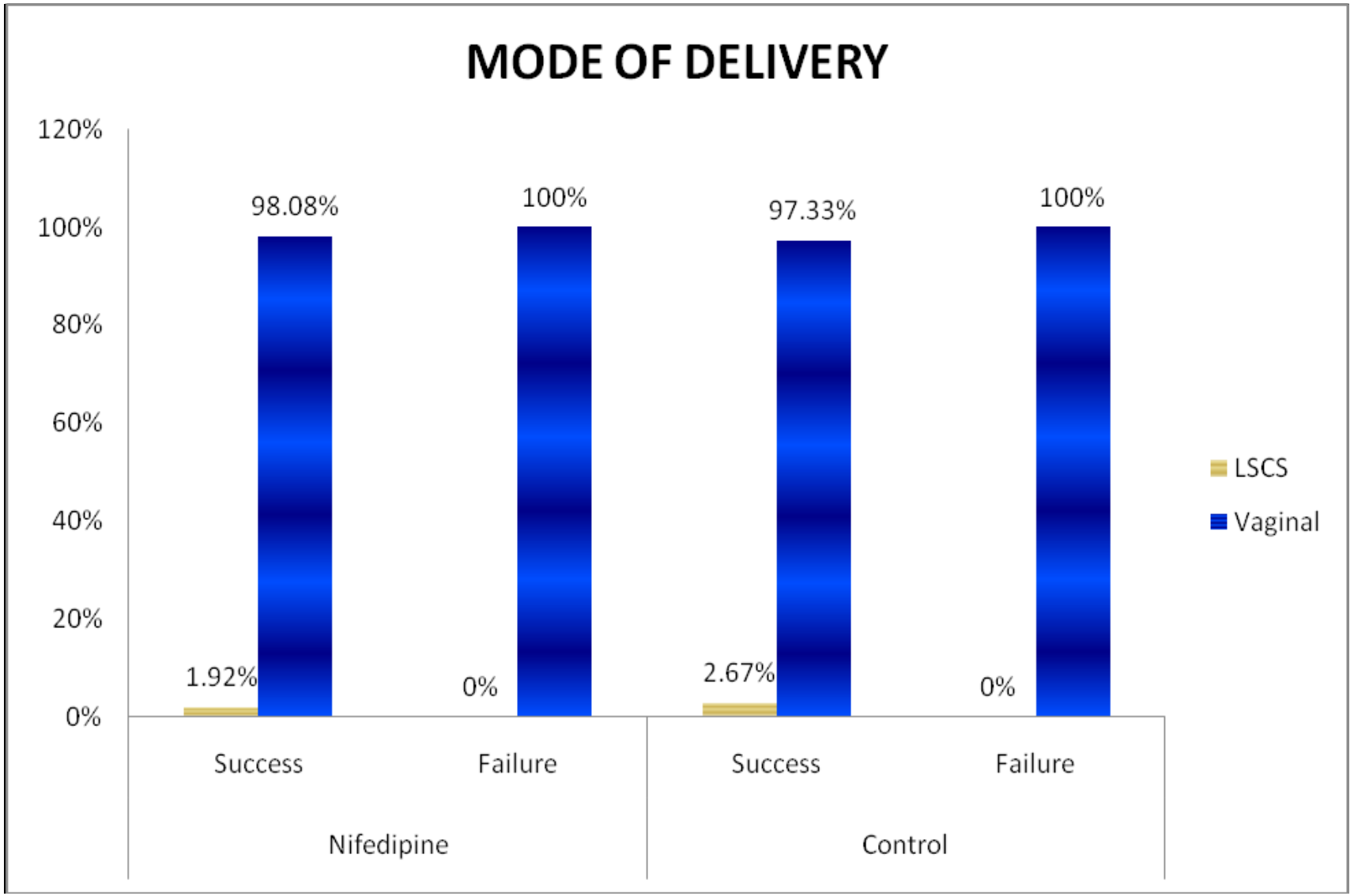
Table :11

Mode of Delivery	Nifedipine				Control			
	Success		Failure		Success		Failure	
	No.	%	No.	%	No.	%	No.	%
LSCS	2	1.92%	0	-	1	2.67%	0	-
Vaginal	73	98.08%	15	100%	51	97.33%	35	100%

98.08% and 97.83 % of cases delivered vaginally in Nifedipine and control success groups respectively. The p value (0.884) was insignificant.

2 cases of Nifedipine group underwent LSCS (Lower Segment Caesarean Section) for PROM (Premature Rupture of Membranes) with no response to oxytocin.

One case in control group underwent LSCS for failed response to oxytocin.

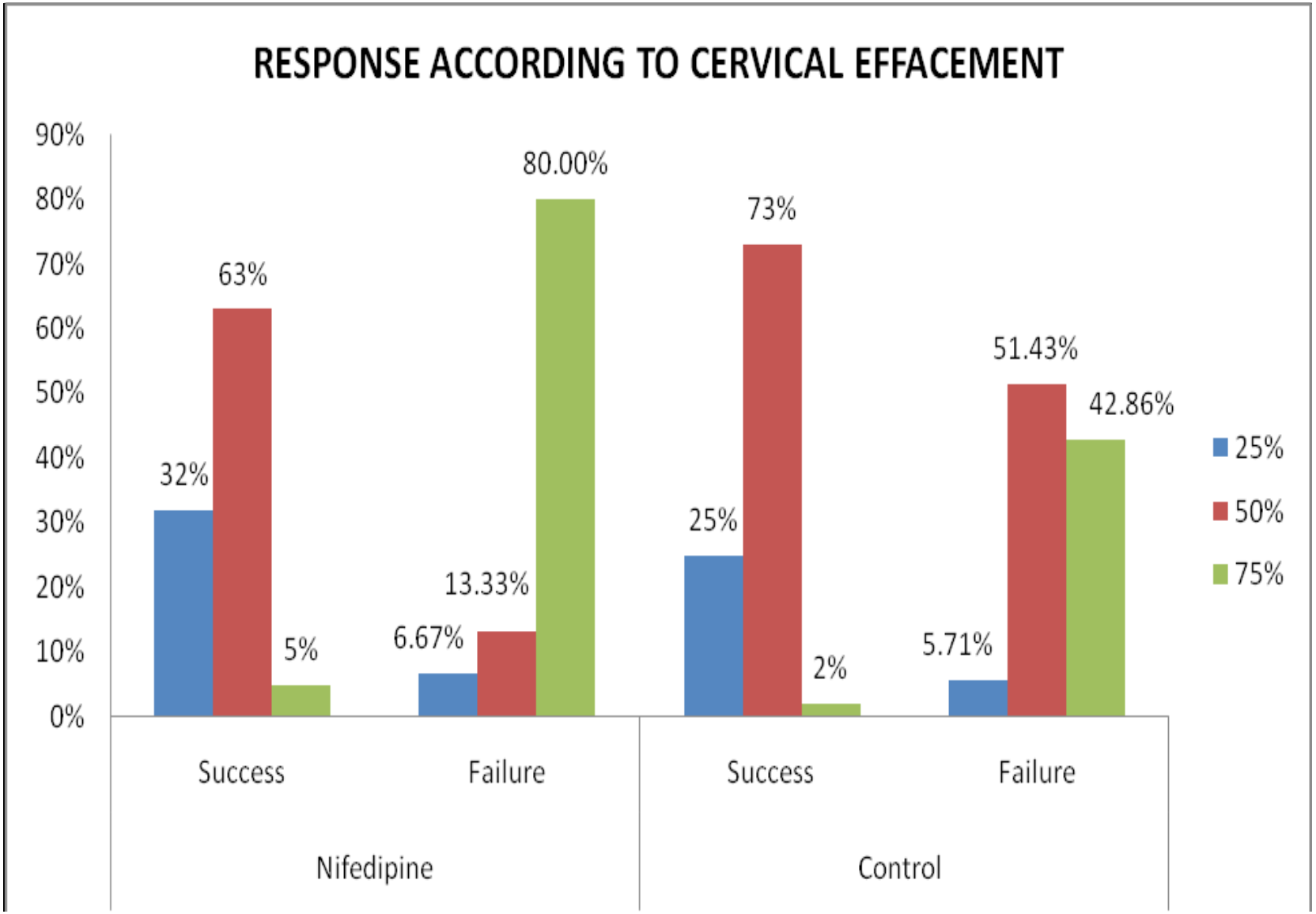

MODE OF DELIVERY
120%
100%
80%
60%
40%
20%
0%
98.08%
100%
97.33%
100%
1.92%
0%
2.67%
0%
Success
Failure
Success
Failure
Nifedipine
Control
LSCS
Vaginal

RESPONSE ACCORDING TO CERVICAL EFFACEMENT

Table:12

P/V Effacement	Nifedipine				Control			
	Success		Failure		Success		Failure	
	No.	%	No.	%	No.	%	No.	%
25%	24	32%	1	6.67%	13	25%	2	5.71%
50%	47	63%	2	13.33%	38	73%	18	51.43%
75%	4	5%	12	80%	1	2%	15	42.86%

Among the patients who delivered successfully in the nifedipine and the control groups cervix was 25% effaced in 32% and 25% and was 50% effaced in 63% and 73.07% respectively. P value 0.233.

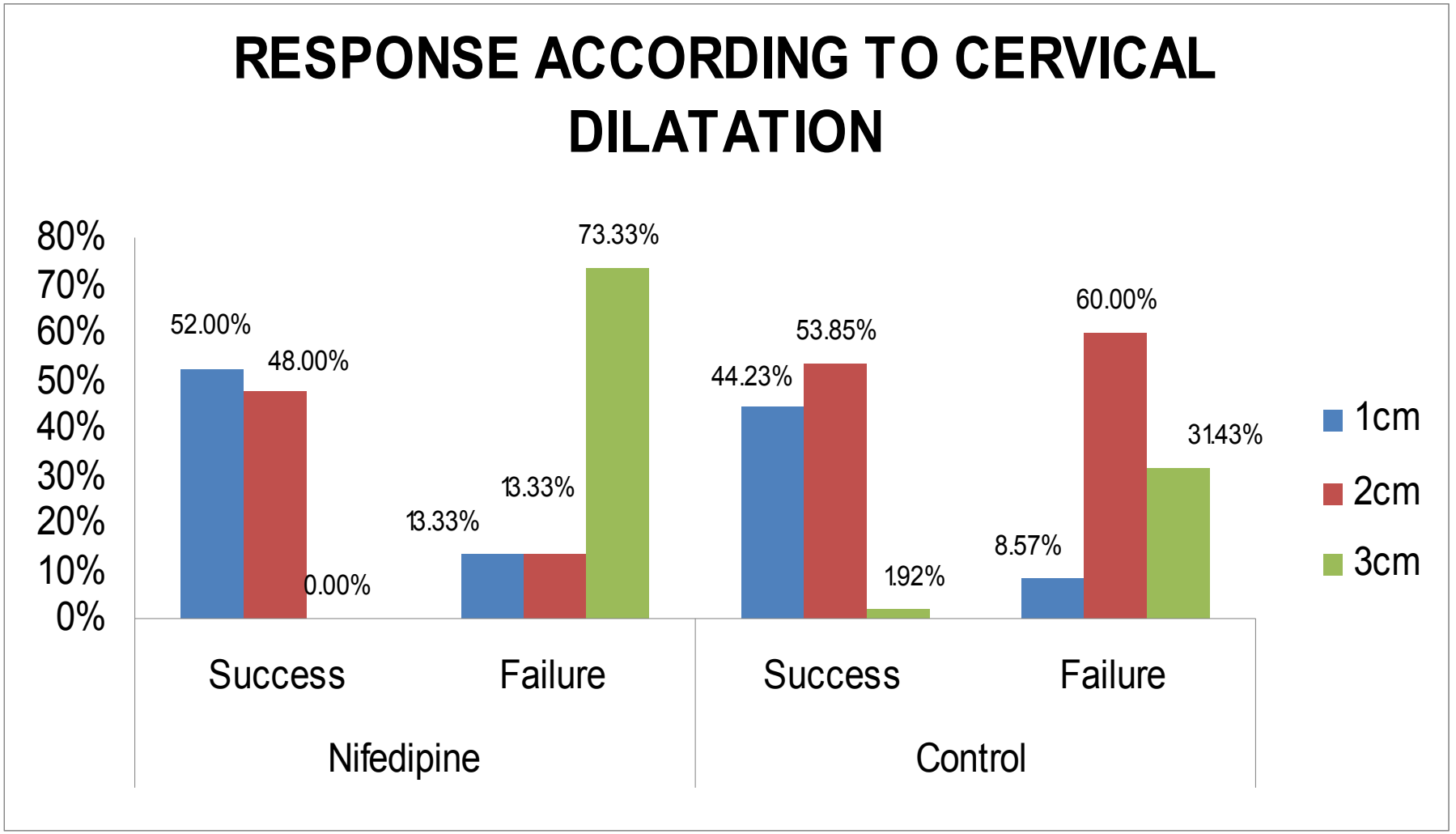

RESPONSE ACCORDING TO CERVICAL EFFACEMENT
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
32%
63%
5%
6.67%
13.33%
80.00%
25%
73%
2%
5.71%
51.43%
42.86%
25%
50%
75%
Success
Failure
Success
Failure
Nifedipine
Control

RESPONSE ACCORDING TO CERVICAL DILATATION

Table :13

P/V Dilatation	Nifedipine				Control			
	Success		Failure		Success		Failure	
	No.	%	No.	%	No.	%	No.	%
1cm	39	52.00%	2	13.33%	23	44.23%	3	8.57%
2cm	36	48.00%	2	13.33%	28	53.85%	21	60.00%
3cm	0	0.00%	11	73.33%	1	1.92%	11	31.43%

The patients who delivered after 48 hours in the nifedipine and control groups had a cervical dilatation of 2cm in 48% and 53.85% and 1cm dilalation in 52% and 44.23 % respectively . P value is 0.138.


RESPONSE ACCORDING TO CERVICAL DILATATION
80%
70%
60%
50%
40%
30%
20%
10%
0%
52.00%
48.00%
0.00%
13.33%
13.33%
73.33%
44.23%
53.85%
1.92%
8.57%
60.00%
31.43%
1cm
2cm
3cm
Success
Failure
Success
Failure
Nifedipine
Control

MATERNAL MORBIDITY

Table :14

Sl.No	Side effects	Number
1	Tachycardia	12
2	Facial flushing	6
3	Headache	19
4	Hypotension	10
5	Nausea & Vomiting	4

There was no maternal mortality. No case of postpartum hemorrhage in those who delivered within 48 hours.

FETAL AND NEONATAL EFFECTS

Fetal tachycardia was observed in 3 cases in Nifedipine group.

NEONATAL MORBIDITY

Table :15

Mode of Delivery	**Nifedipine**		**Control**	
	Success	Failure	Success	Failure
Birth asphyxia	-	1	2	2
RDS	1	3	3	6
Septicaemia	-	2	1	4
IVH	1	1	1	2
Congenital anomalies	-	-	-	1

Better neonatal outcome as to the decrease in the presence of Respiratory Distress Syndrome (RDS) and other complications in neonates is more in Nifedipine success group.

NEONATAL MORTALITY

Table :16

S.No	Neonatal Mortality	Nifedipine (90)		Control (87)	
		Success	Failure	Success	Failure
1	Vaginal	2 (2.6%)	4(26.3%)	4(7.6%)	10(28.57%)
2.	Caesarean section	-	-	-	-

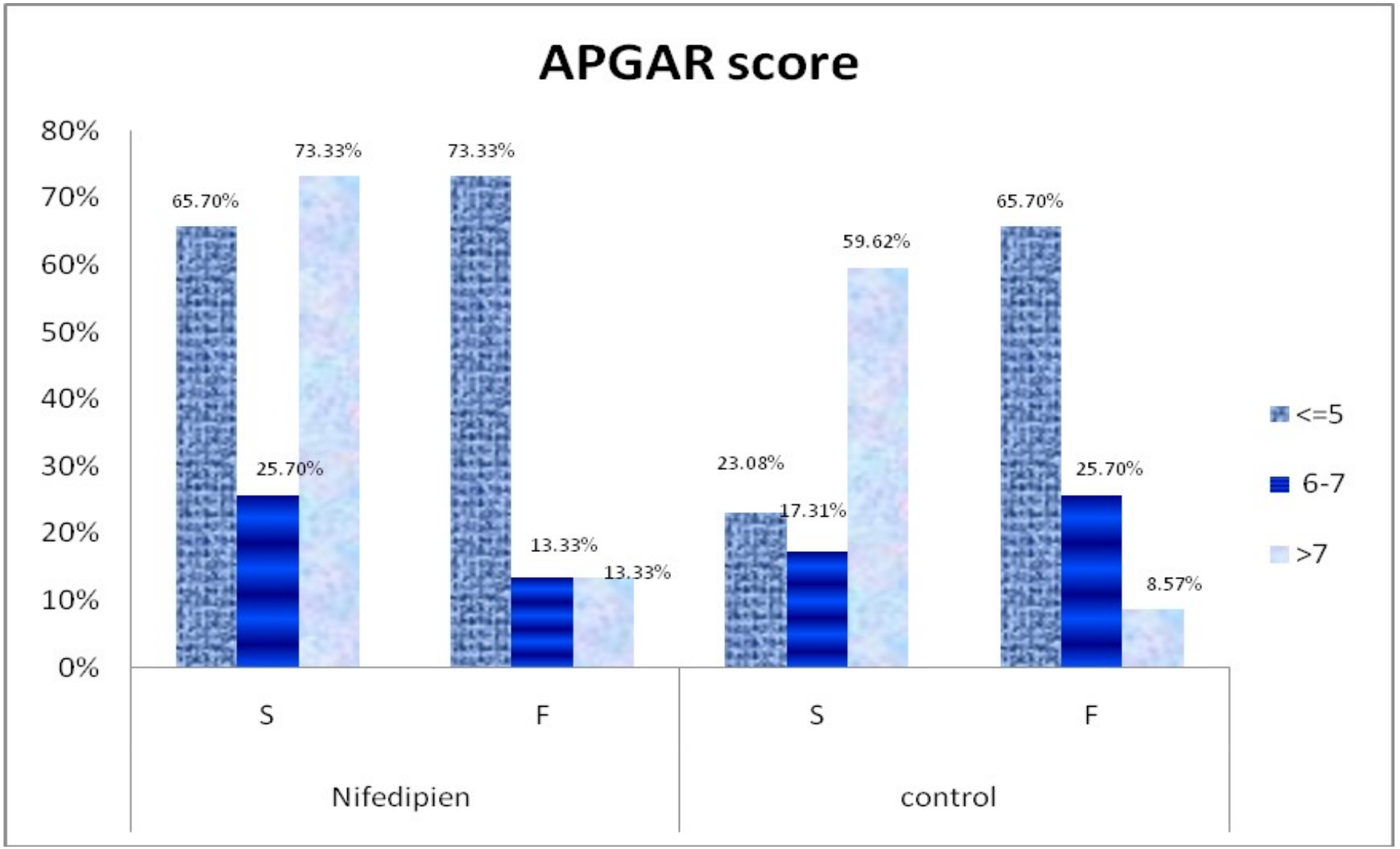
The neonatal mortality was observed in 26.3% and 28.57% of failure cases delivered vaginally with Nifedipine and control groups respectively. No neonatal mortality was observed in caesarean group.

APGAR SCORE

Table: 17

S.No	5' Apgar	Nifedipine				Control			
		S		F		S		F	
		No.	%	No.	%	No.	%	No.	%
1	≤5	2	2.67%	11	73.33%	12	23.08%	23	65.7%
2	6-7	18	24%	2	13.33%	9	17.31%	9	25.7%
3	>7	55	73.33%	2	13.33%	31	59.62%	3	8.57%

73.33 % and 59.62% who delivered successfully after 48 hours had Apgar of >7 in nifedipine and control groups respectively, the p value was significant 0.000.

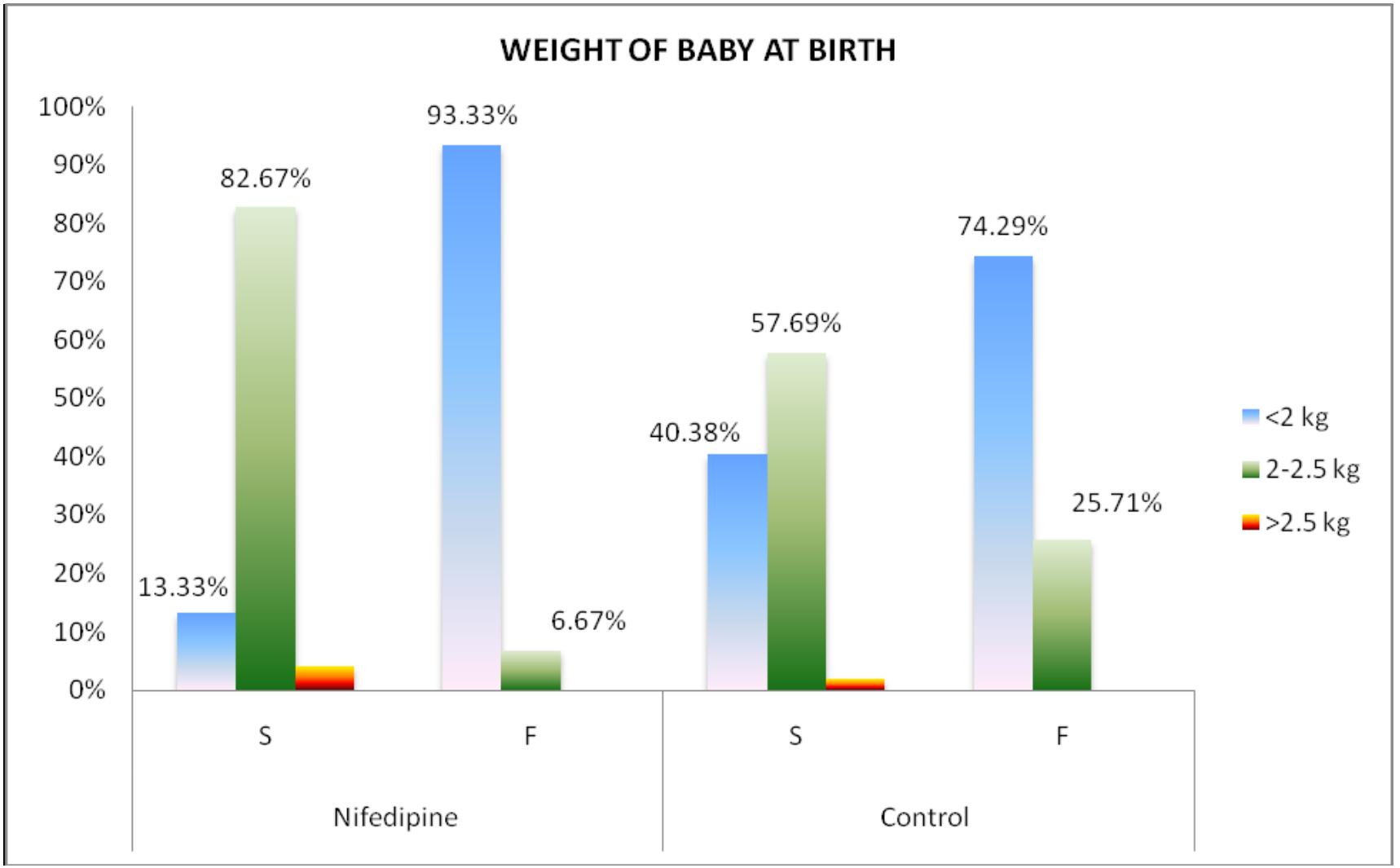

APGAR score
80%
70%
60%
50%
40%
30%
20%
10%
0%
65.70%
25.70%
73.33%
73.33%
13.33%
13.33%
23.08%
17.31%
59.62%
65.70%
25.70%
8.57%
S
F
S
F
Nifedipien
control
<=5
6-7
>7

WEIGHT OF BABY AT BIRTH

Table : 18

Birth weight (kg)	Nifedipine				Control			
	S		F		S		F	
	No.	%	No.	%	No.	%	No.	%
<2	10	13.33%	14	93.33%	21	40.38%	26	74.29%
2-2.5	62	82.67%	1	6.67%	30	57.69%	9	25.71%
>2.5	3	4.00%	0	-	1	1.92%	0	-

Among the success cases 82.67% in Nifedipine groups had birth weight of 2-2.5kg compared to 57.69% in control success group. 4% in nifedipine success group had birth weight of >2.5kg compared to 1.92% in control success groups. P value is .001 which is significant.

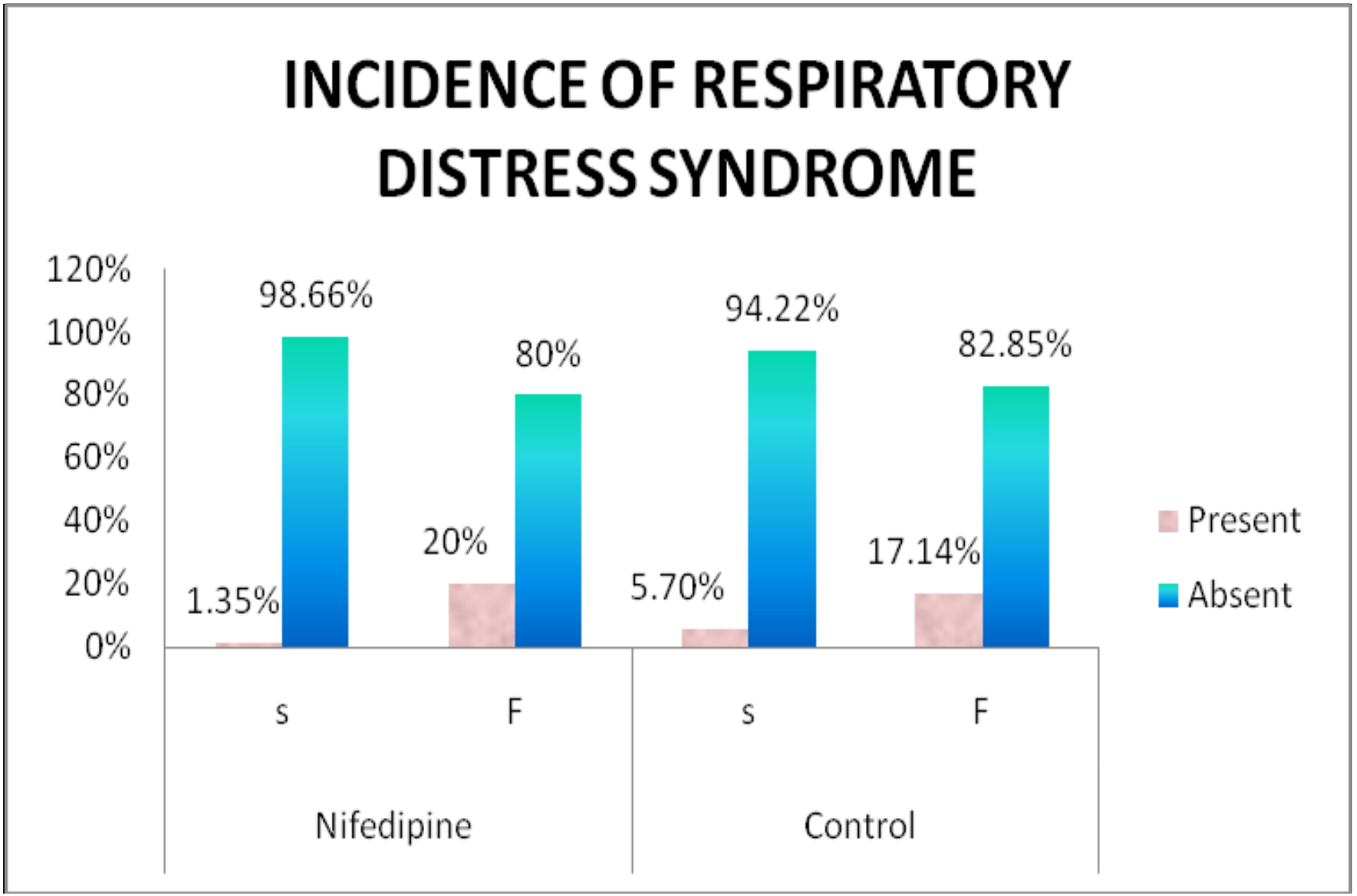

WEIGHT OF BABY AT BIRTH
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
13.33%
82.67%
6.67%
93.33%
40.38%
57.69%
25.71%
74.29%
<2 kg
2-2.5 kg
>2.5 kg
S
F
S
F
Nifedipine
Control

INCIDENCE OF RESPIRATORY DISTRESS SYNDROME

Table :19

RDS	Nifedipine				Control			
	Success		Failure		Success		Failure	
	No.	%	No.	%	No.	%	No.	%
Present	1	1.35%	3	20%	3	5.7%	6	17.14%
Absent	74	98.66%	12	80%	49	94.22%	29	82.58%

The incidence of RDS is 1.35% in nifedipine success group and 5.7% in control success group (P value is 0.046).


INCIDENCE OF RESPIRATORY DISTRESS SYNDROME
120%
100%
80%
60%
40%
20%
0%
98.66%
80%
94.22%
82.85%
1.35%
20%
5.70%
17.14%
Present
Absent
s
F
s
F
Nifedipine
Control

DISCUSSION

DISCUSSION

In our study the range of gestational age was 28 to 34 weeks.In other studies it was 24 to 32 weeks (Nikolov et al) and 26 to 34 weeks (Bekkari et al). In Cochrane metaanalysis by King JF et al in 2003, the inclusion range of gestational age was from 20 to 26 weeks upto a maximum of 33.5 to 36 weeks.The trials in the metaanalysis excluded women with cervical dilation more than 4cm, while in our study the limit was 3cm.

In our study the dosage of Nifedipine used is 30mg of loading dose given as 10 mg tablets every 20 minutes followed 3 hours later by a maintenance dose of 10 mg of oral nifedipine 6 hourly for 3days. Similar to this a loading dose of oral nifedipine 3×10mg was used by Bekkari et al .A loading dose 4×10 mg of oral nifedipine was used by Nikolov et al in their study.

In Cochrane metaanalysis in 2003,the maximum dose used was 40 mg of oral Nifedipine in the first hour followed by 20mg of slow release Nifedipine at t=90 minutes(Papatsonis et al).

Most of the trials in the Cochrane metaanalysis 2003 measured outcome primarily by delay in delivery for more than 48 hours as in our study.9 out of 13 trials in this review reported a favourable outcome.Bekkari et al and Nikolov et al reported a success of 84% and 86.4% respectively, while in our study it was 83.33%.

Mean duration of prolongation of pregnancy in the Nifedipine group in the Cochrane metaanalysis was 3.83days while in our study it was 3.78days.

The most common side effects in the trials in Cochrane metaanalysis were hypotension and headache similar to our study.Similar to our study there was no maternal mortality in any of those trials .No maternal side effects and good patient tolerance were reported by Nikolov et al and Bekkari et al respectively in their studies.

Similar to our study there was a reduction in respiratory distress syndrome and improved Apgar scores at 5minutes in Cochrane meta-analysis 2003.

SUMMARY

SUMMARY

In the study with Nifedipine n-90 control n=87 it was observed that.

1) Preterm labour was common in primigravida in the age group 20- 29 years, belonging to lower socioeconomic status and who did not receive appropriate antenatal care.
2) There were 71% of cases between 31& 34 weeks.
3) Previous preterm delivery was found in 8.3% ,previous abortions was found in 5.5% and physical stress like manual work travelling was found in 33.8% of the patients.
4) The success of Nifedipine as indicated by prolongation of pregnancy beyond 48 hours was observed in 83.33% of cases compared with 59.77% in controls. P value was significant(0.000)
5) Nifedipine dose 20mg was required in 52% of paitents, 30mg in 34.66% of patients and 10mg in 13.33% of patients to stop contractions.
6) The prolongation of pregnancy more than 48 hours was found to be more in 31-34 weeks of gestational age in nifedipine and control groups.

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7) The cervix was 1cm dilated in 45.55% and 29.88% , 2cm dilated in 42.22% and 56.32% and 3cm dilated in 12.22% and 13.79% in nifedipine and control groups respectively.

8) The patients who delivered after 48 hours in the nifedipine and control groups had a cervical dilatation of 2cm in 48% and 53.85% and 1cm dilalation in 52% and 44.23 % respectively. P value is 0.138.

9) The cervix was 25% effaced in 27.78% and 17.24% of cases ,50% effaced in 54.44% and 64.37% of cases and75% effaced in 17.78% and 18.39% of cases in nifedipine and control group respectively

10) Among the patients who delivered successfully cervix was 25% effaced in 32% and 25% and was 50% effaced in 63% and 73% of Nifedipine and control groups respectively

11)Headache and maternal tachycardia were the commonest side effects observed.

12)The was no maternal mortality

13)Fetal mortality was due to complications of prematurity. Fetal tachycardia was observed in 3 cases.

14)The percentage of cases delivered vaginally in Nifedipine and control success group were 79.3% and 98% respectively.

15)73.33 % and 59.62% of neonates of patients who were delivered successfully after 48 hours had Apgar of >7 in nifedipine and control groups respectively, the p value was significant 0.000.

16)Among the success cases 82.67% in Nifedipine groups had birth weight of 2-2.5kg compared to 57.69% in control success group. 4% in nifedipine

success group had birth weight of >2.5kg compared to 1.92% in control success groups. P value is .001 which is significant.

17) The incidence of RDS is 1.35% in nifedipine success group and 20% in nifedipine failure group compared to 5.7% in control success group and 14.3% in control failure group (P 0.046).Better neonatal outcome as to the decrease in the presence of RDS and other complications in neonates is more in nifedipine success group.

CONCLUSION

CONCLUSION

Labour inhibiting drugs may not treat the cause of preterm labour but they only treat the symptoms, that is contractions.

As these agents make the uterus refractory to contractile stimuli for a short time so that the perinatal outcome is improved. In this clinical study idiopathic spontaneous preterm labour whose onset was at 28 to 34 weeks has responded well to tocolytic therapy by oral nifedipine and neonatal outcome improved and no maternal mortality was observed. The maternal side effects were reversed on discontinuation of the drug. The drug has provided the fetus of its valuable opportunity of being inside the mothers womb for a period enough to make the lungs mature by administration of exogenous steroids.

However decrease in the incidence of preterm labour lies in identification of high risk patients, improving the socio- economic standards, better antenatal care, education and early detection of the onset of labour.

In developing countries neonatal intensive care are usually found in tertiary referral hospitals but not all such units have the required treatment capabilities. The statistically significant benefits of nifedipine in suppressing

the uterine contractions for in utero transfer,in reducing neonatal respiratory distress syndrome along with its reduced maternal side effects, and its low cost makes it to be considered as the first line tocolytic agents in these countries.

PROFORMA

PROFORMA

Name

Age

IP.No

Unit

Gravida

Para

Last Menstrual Period (LMP)

Live

Expected Date of Delivery (EDD)

Abortion

Corrected EDD (C.EDD)

SES

Menstrual cycle

Occupation

Height

Residence

Weight

Booked /Unbooked (UB)

Immunized / Not

DOA (Date of Admission)

Duration of Hospital stay

DOD (Date of Discharge)

Period of gestation

Present complaints

Lower abdominal pain

Dull low backache

Vaginal discharge

Fluid leaking per vaginum

Fever

UTI (Urinary Tract Infection)

URI (Upper Respiratory Tract Infection)

Bleeding

Obstetric history

I. Trimester

- Hyperemesis
- Exanthematous fever
- Bleeding
- Radiation exposure
- Medication
- Pain abdomen

II. Trimester

- Date of Quickening
- Bleeding per vaginum
- History of (H/O) PIH
- H/O GDM (Gestational Diabetes Mellitus)

III. Trimester

- Bleeding per vaginum
- UTI

Cervico vaginal infection

Coitus

Diabetes

Hypertension

Fever

Trauma

Past obstetric history

Previous child birth

H/O abortion

H/O Preterm labour

H/O Babies with congenital anamolies

Past Medical History

Tuberculosis

Bronchial Asthma

STD (Sexually Transmitted Diseases)

Jaundice

Renal disease

Heart disease

Diabetes mellitus

Epilepsy

General examination

Temperature (T) Pallor Pedal edema

PR BP RR RS CVS

Obstetric examination

Per Abdomen ;-

Fundal height

Symphysio fundal height

Contractions

Presentation

Position

Liquor

FHR (Fetal Heart Rate)

Expected Fetal Weight at admission

Weight after birth

Per Vaginal Examination (P/V)

Cervix

Membranes

Pelvis

Investigations

Urine analysis

Urine culture sensitivity

Complete Blood Count

Blood urea,

Sugar

S. Creatinine

S. Electrolytes

ECG

USG Abdomen

Nifedipine

Time	Dose	Contractions	T	PR	BP	RR	FHR	P/V

Side effects

Period of tocolysis

Mode of delivery

Fetal Outcome

Birth weight

Apgar

Neonatal complications

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MASTER CHART